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OF
OPHTHALMOLOGY

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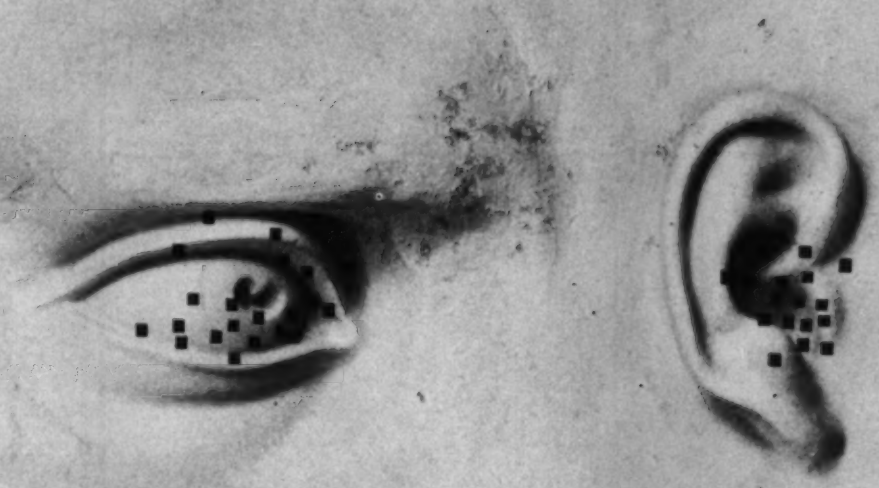

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1. Gordon, D. M.: Scientific Exhibit, American Medical Association, Annual Meeting, San Francisco, 1958.

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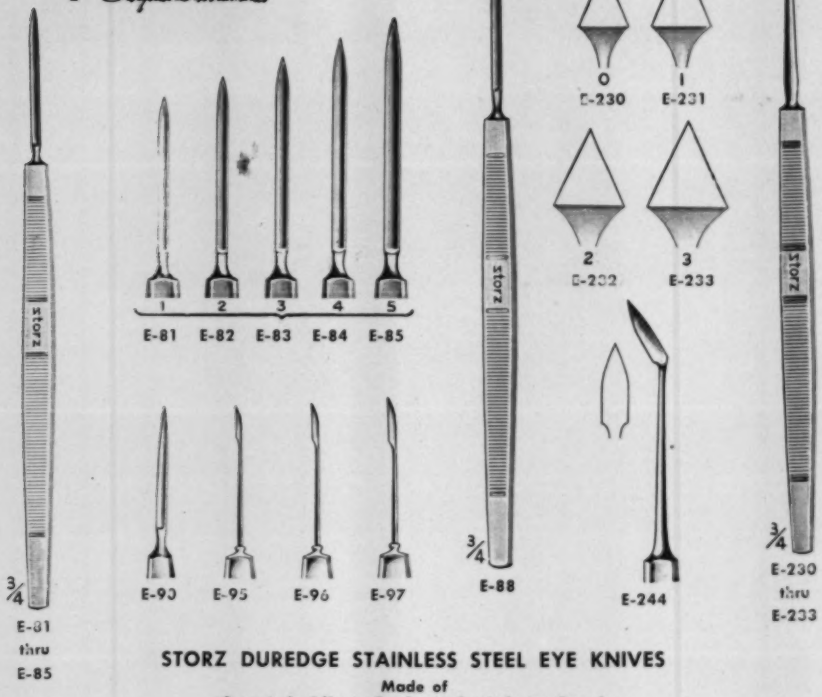

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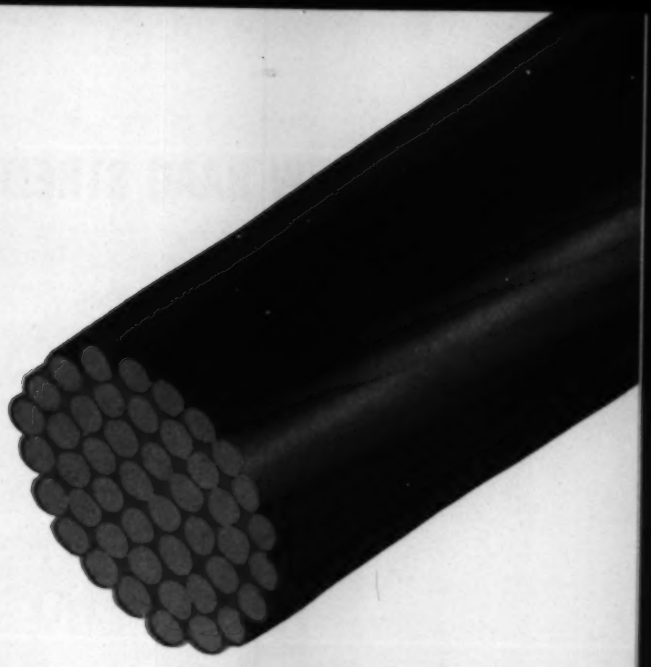

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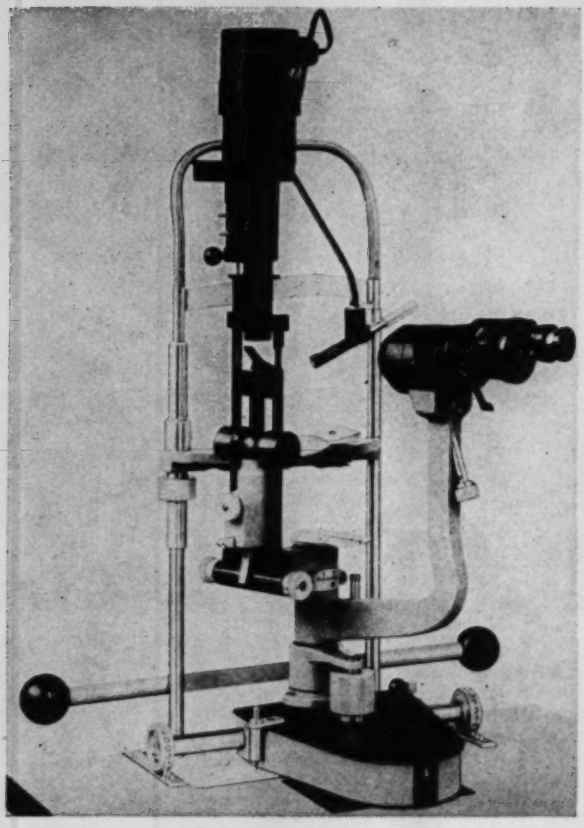

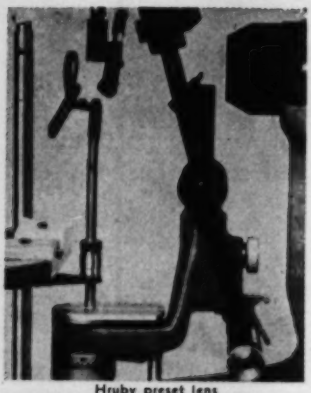

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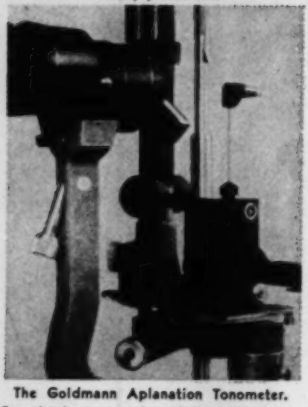

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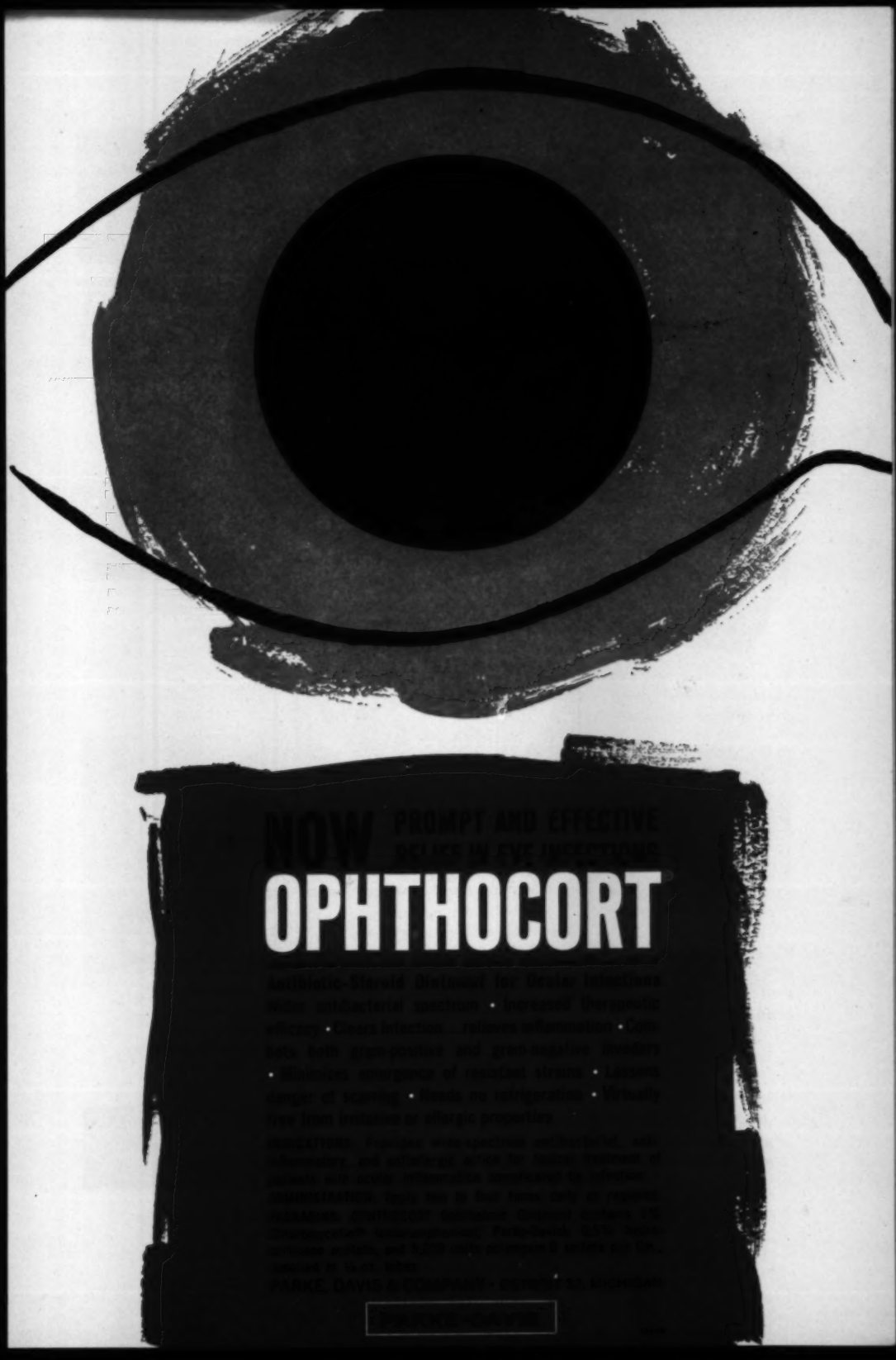
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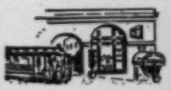

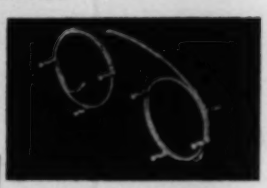

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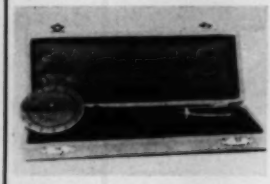

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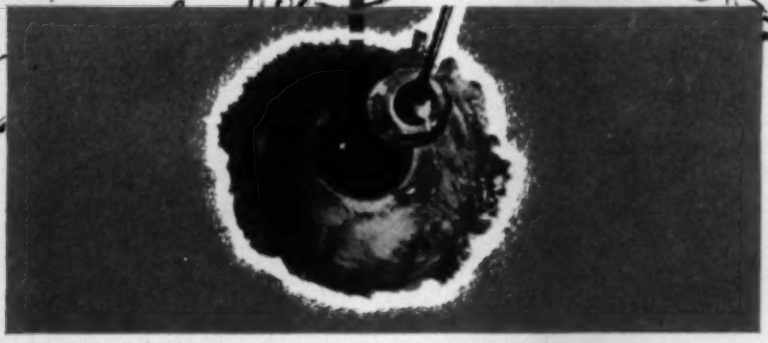

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1. Thorpe, H. E.: Am. J. Ophth. *49*:531-547 (Mar.) 1960. 2. Schwartz, B., *et al.*: Tr. Am. Acad. Ophth. & Otol. *64*:46-54 (Jan.-Feb.) 1960. 3. Cogan, J. E. H.: Proc. Roy. Soc. Med. *51*:927, 1958. 4. Jenkins, B. H.: J.M.A. Georgia *45*:431, 1956. 5. Raiford, M. B.: J.M.A. Georgia *48*:163, 1959. 6. Rizzuti, A. B.: Arch. Ophth. *61*:135, 1959.

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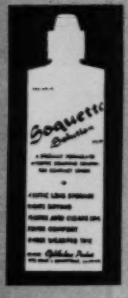

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[1] CLIFTON, C. E. AND HALL, N. C. "RE-STERILIZING ACTIVITY OF CERTAIN CONTACT LENS SOLUTIONS." CONTACTO, THE CONTACT LENS JOURNAL, 3:10, 301-2, 1959.

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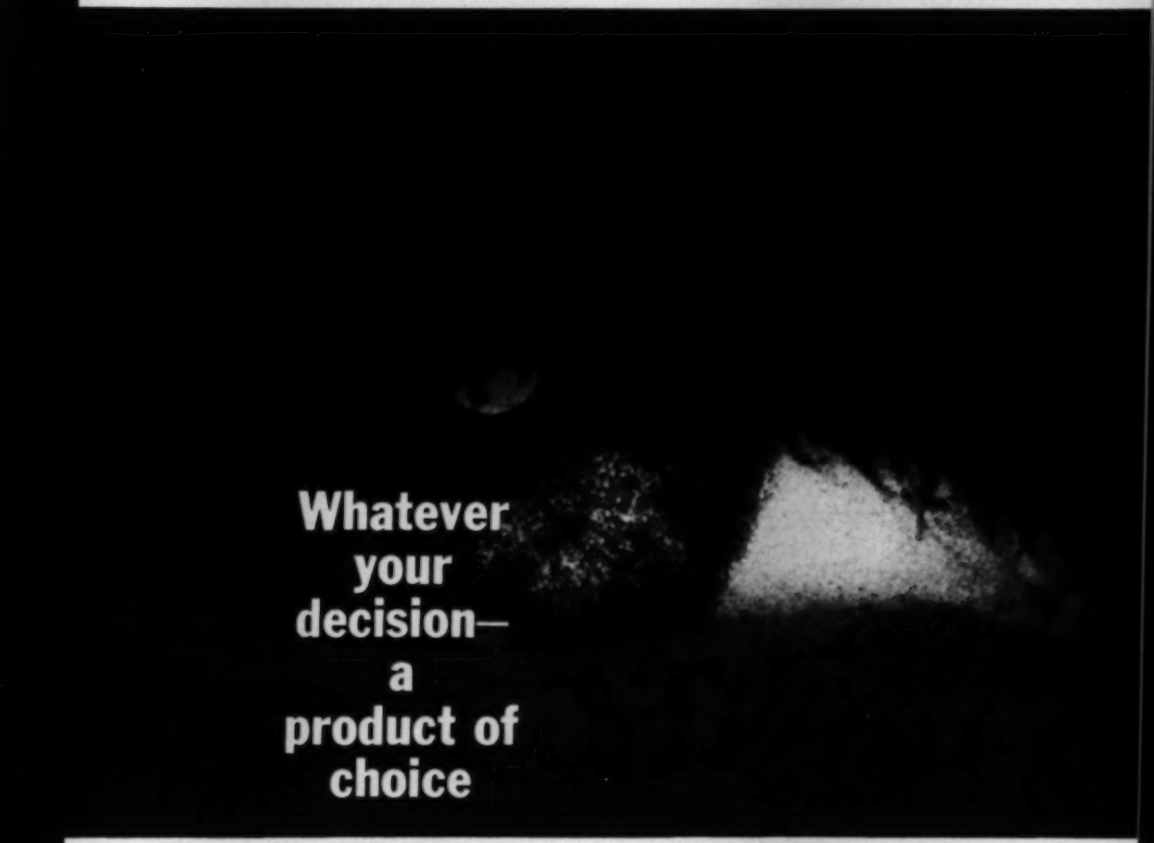

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- no additives

In Ocular Surgery...

THE PERFECTED
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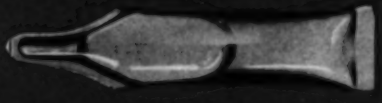

disposable single dose

guarantees
sterility and stability
AT THE MOMENT OF USE

Avoid Pyocyaneus Infection

USE
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sterile fluorescein applicators

For delineating corneal injuries.
For determining site of intraocular injury.
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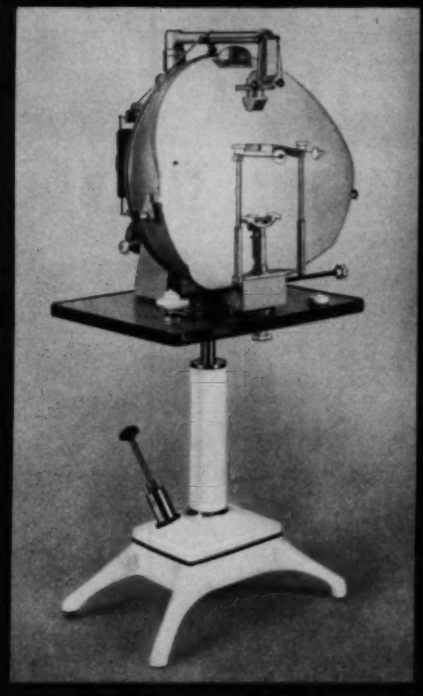

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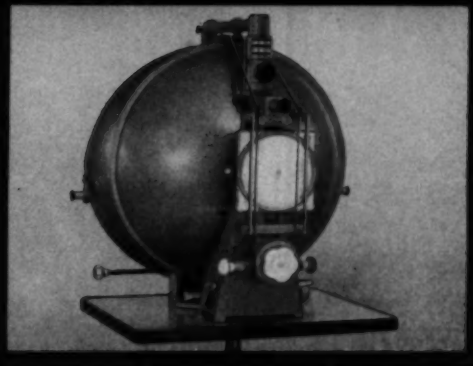
the new

HEMISPHERIC PROJECTION PERIMETER

with automatic recording



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- Projection of test marks in white, green, red, yellow and blue—sizes: 9; 4.5; 2.25 and 1.12 mm.
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- Mounted on a beautiful, sturdy instrument table with unique hydraulic system for elevation and lowering.

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Gantrisin Diethanolamine Ophthalmic Solution and Ointment contain 4% Gantrisin®—brand of sulfisoxazole.

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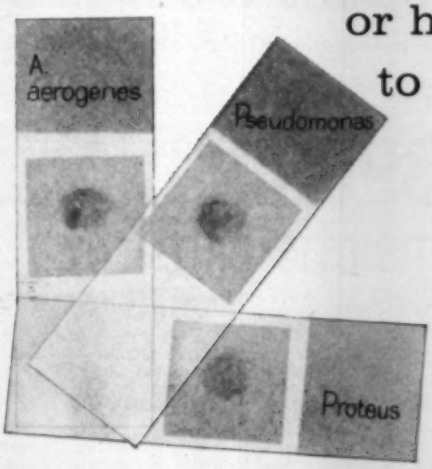
DECLOMYCIN NOTES:

Demethylchlortetracycline Lederle

pathogen

sensitivity

In addition to the expected broad-spectrum range of effectiveness, DECLOMYCIN has demonstrated activity against strains of Pseudomonas, Proteus and A. aerogenes[1-4] unresponsive or highly refractory to other antibiotics.



1. Finland, M.; Hirsch, H. A., and Kunin, C. M.: Read at Seventh Annual Antibiotics Symposium, Washington, D. C., November 5, 1959. 2. Hirsch, H. A.; Kunin, C. M., and Finland, M.: **München. med. Wchnschr.** To be published. 3. Roberts, M. S.; Seneca, H., and Lattimer, J. K.: Read at Seventh Annual Antibiotics Symposium, Washington, D. C., November 5, 1959. 4. Vineyard, J. P.; Hogan, J., and Sanford, J. P.: **Ibid.**

Capsules, 150 mg.—Pediatric Drops, 60 mg./cc. — New Syrup, cherry-flavored, 75 mg./5 cc. tsp., in 2 fl. oz. bottles—3-6 mg. per lb. daily in four divided doses.

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- their wide-spectrum bactericidal activity includes *ALL clinically isolated strains of Pseudomonas aeruginosa*, a serious invader noted for the rapidity of its destructive powers.
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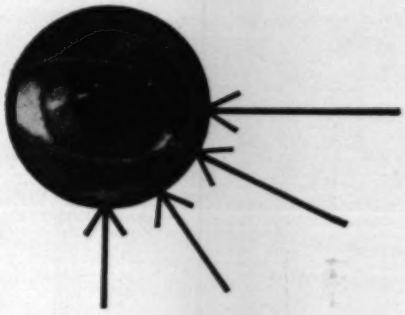

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DYCLONE™

rated highly for office use[1]

considered outstanding in ophthalmic surgery[2]

rapid

• produces anesthesia within 2-5 minutes. ...duration of anesthesia 30 to 50 minutes.[2]

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• clinical evaluation studies in various medical specialties (more than 5000 patients) showed a sensitivity of less than 1/10 of 1%. • rarely causes irritation. • no influence on pupillary size.

antibacterial

• significant antibacterial action.[3]

Dyclone Solution 0.5 per cent, bottles of 1 and 8 oz.

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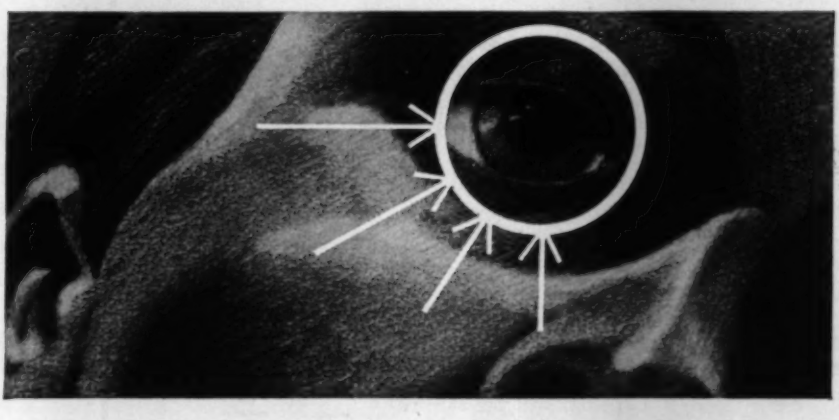
1. Swan, K. C.: Tr. Am. Acad. Opth. *60*:368, 1956.
2. Arora, R. B., et al.: E. E. N. T. Monthly *34*:593, 1955.
3. Florestano, H. J., and Bahler, M. E.: J. Am. Pharm. A. (Scient. Ed.) *45*:360, 1956.



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An area of service as satisfying to the practitioner as it is rewarding to the patient.
T/O Kit of Safety Eyewear helps practitioner prescribe *protection*, where needed, as well as correction.

Many of your patients—do-it-yourselfers, carpenters, plumbers, etc.—are exposed to eye hazards at work, at home, at play, and *need* a second pair for safety.

You are their only chance of getting this protection, in most cases. Does your patient history investigation explore possible need of safety eyewear?

You have a wonderful opportunity for service to your patients and your community in prescribing for protection as well as correction.

TAKE THESE 3 STEPS NOW:

1. Inquire into all patients' need of a *second pair for safety.*
2. Order from your independent supplier a Titmus Safety Eyewear Kit of samples.
3. Wear safety glasses *in your own* avocations where eye hazards may occur . . . as an example to others.

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"The Golden Link to Complete Service"

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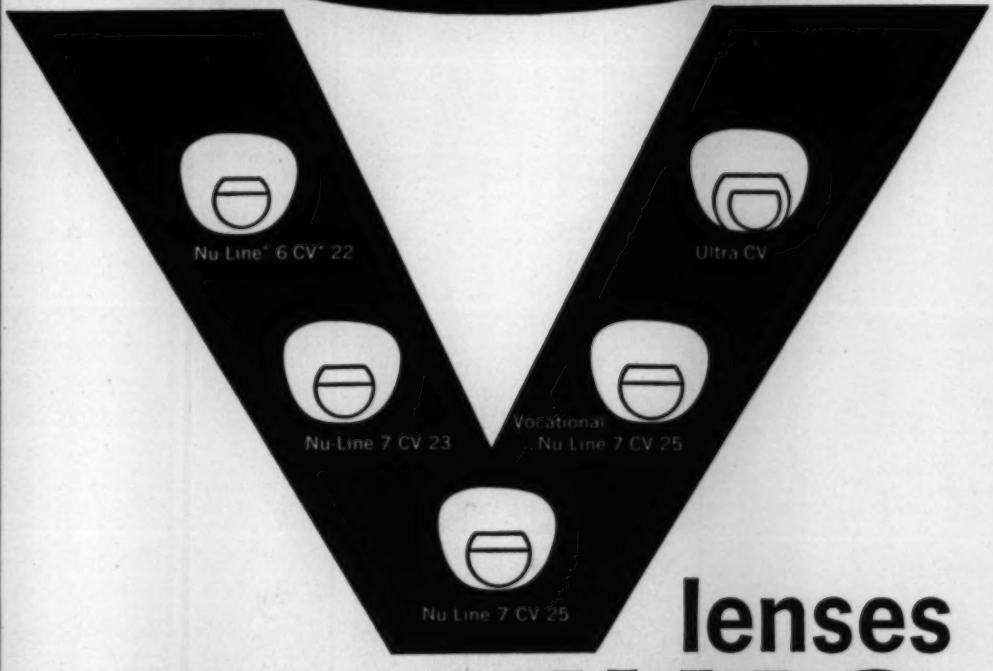
the only way
to get Excellity* performance
in the area 18″ to 50″
from the eyes—
UNIVIS Nu-Line Continuous Vision*
lenses



lenses
UNIVIS

IDENTIFIED—Look for the faint brownish-pink coloration* of the segment line

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With the fused
Panoptik Lenticular
Cataract lens

No aphakic patient of yours need

worry about his appearance

Put an end to your aphakic patient's concern for his appearance when he gets his new glasses. Fit him with the "crown jewel of ophthalmic lenses."

The Panoptik Lenticular Cataract has a continuous front surface, like any fused bifocal. There is no bulbous protrusion in the lenticular area to gather highlights and shadows. Viewed obliquely, or from the side, the lenticular field and reading segment tend to disappear altogether.

The PLC is a flatter, thinner, lighter lens, because of the special Bausch & Lomb glass combination. Center thickness is 2mm less than that of a corresponding lens in regular crown glass thus reducing its weight.

And the PLC is as much a treat for the doctor as it is for the patient. It provides wide latitude in power range and segment location. It's a satisfaction to prescribe and fit. Optical centers are easy to locate where they belong, and the distance field has all the diameter required, between 28 and 32mm. In certain cases where an adjustment of the original position may be necessary, lenses may be resurfaced because the reading segment is located between the carrier and the distance field.

For your own examination, and for help in explaining lens function to patients, an actual cross-section sample of a Panoptik Fused Lenticular Cataract lens is yours for the asking. Mail the coupon below.

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Sirs: Please send, without obligation, one of your sample cross-section PLC lenses.

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When your single-vision Rx lenses you know you will obtain quality you want in edge and centering, surface quality and

specifies Shuron Widesite

corrected curve lenses with the

center thickness, focus accuracy,

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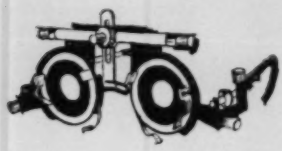
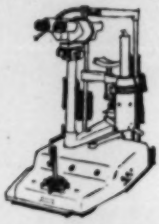
TITMUS INSTRUMENTS AND EQUIPMENT WILL INCLUDE



TRIAL FRAMES
adults and children

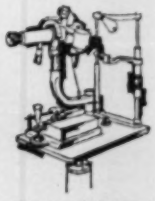
OPHTHALMOSCOPES
(binocular
indirect, direct)

SLIT LAMPS

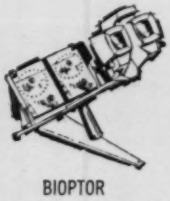


GONIOSCOPY LENSES

FOCIMETERS



OPHTHALMOMETERS



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All Titmus instruments, proved in widespread use here and abroad, meet the highest professional standards.

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THE EYES OF COLLEGE STUDENTS HAVE TO WORK HARD
WHEN THEY NEED HELP—THEY NEED THE BEST

See Your

EYE PHYSICIAN

Then Your

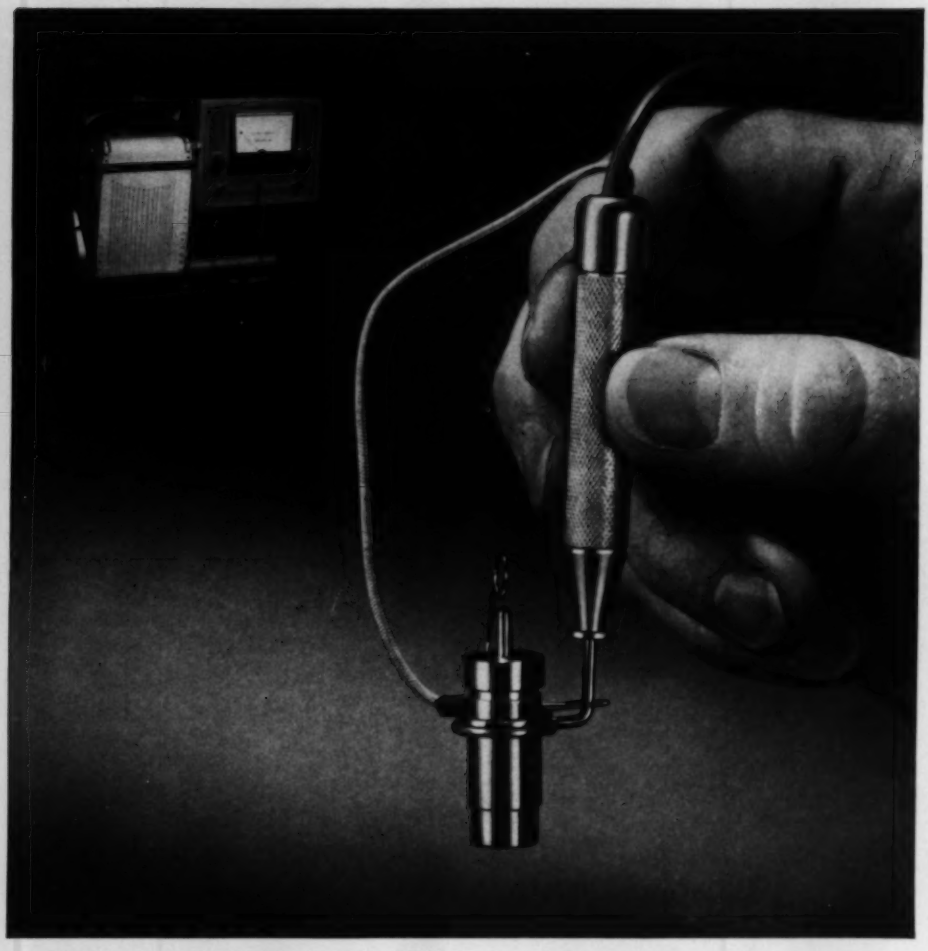
GUILD OPTICIAN

GUILD of PRESCRIPTION OPTICIANS of AMERICA

THE EYE PHYSICIAN—because he is a physician who will understand the problems of overworked eyes in relation to the whole health of the student, under special pressures and demands during these years.

THE GUILD OPTICIAN—because his special training means accurately filling the ophthalmologist's prescription and beyond that, he will take into consideration special study needs and smart styling. In addition, he will always be readily available for after-care and repair for the life of the glasses.

ONE OF A SERIES OF EDUCATIONAL MESSAGES SPONSORED BY THE GUILD OF PRESCRIPTION OPTICIANS OF AMERICA, INC.



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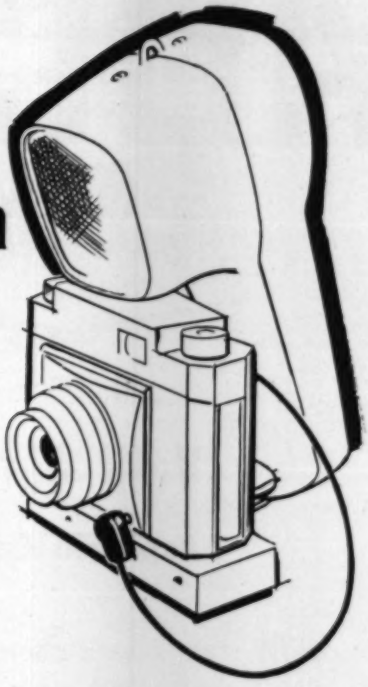
new portable transistor Clini Camera

only $195



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The famous J-D Clini Camera "F", powered by 120v. A.C., is also available at $150.00.

Write for complete information about the exclusive Jenkel-Davidson Clini Cameras. No obligation.

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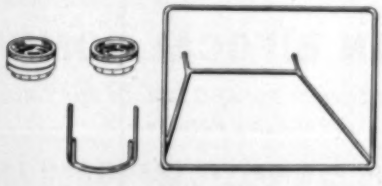

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***NOW** Your Aphakic Patients Can Have Clear*
Side Vision to: Park easily... Use the mirror...
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AMERICAN BIFOCAL COMPANY, INC.

Producers of Straight Top ABC Bifocals and Trifocals
For Every Purpose

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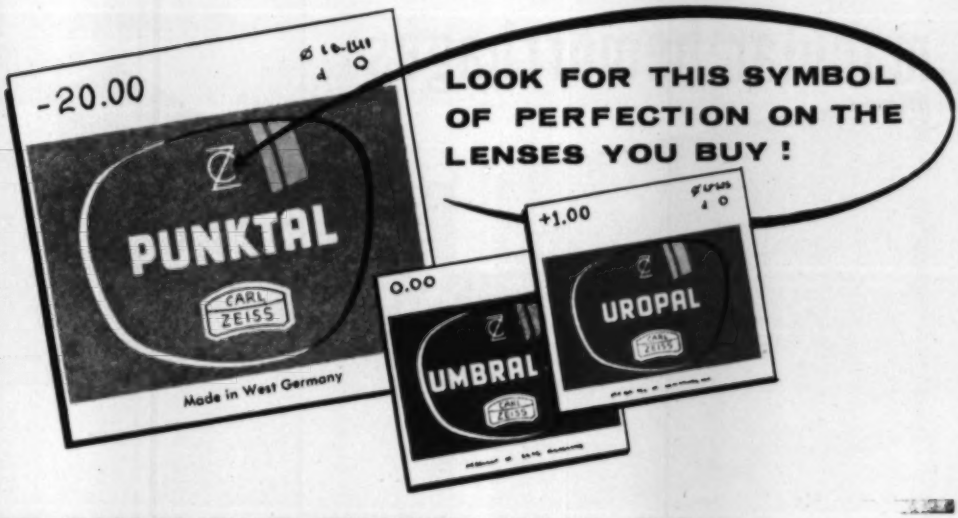


IF ONLY THE FINEST WILL DO . . .

prescribe ZEISS *lenses*

• ZEISS PUNKTAL . . . Crystal clear white lenses with the highest degree of correction, utilizing fully the physiological optical efficiency of the eyes.

• ZEISS UROPAL . . . the only lenses with imperceptible tint that absorbs the harmful infra red rays and is the ultimate for use under artificial light because they control the glare to the eyes.

• ZEISS UMBRAL . . . Fully corrected curve lenses for BEST sun and glare protection. Umbral lenses filter out infra-red and ultra violet rays, have uniform density of color to the outer edges of the lenses and subdue the light of the entire visible spectrum uniformly without impairing the harmony of natural colors.

FOR THE BEST COMBINATION recommend **MARWITZ FILURA** frame for men and **FILURETTE** for ladies . . . the only frames with cosmetic look that give full field of vision.

SEND FOR LITERATURE!

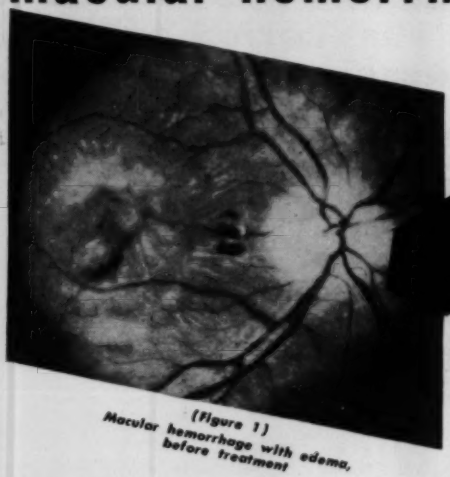
TRANS-CONTINENTAL OPTICAL CORP.

2315 BROADWAY, NEW YORK 24, N.Y.

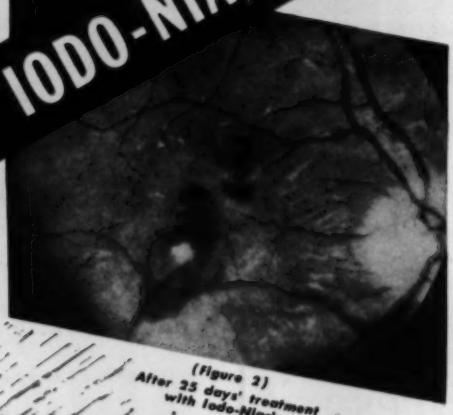
macular hemorrhages

respond to

IODO-NIACIN*



(Figure 1)
Macular hemorrhage with edema, before treatment



(Figure 2)
After 25 days' treatment with Iodo-Niacin

NO IODISM

Macular and retinal hemorrhages are satisfactorily absorbed after use of IODO-NIACIN[1]. The dosage used in this study was 1 tablet three times daily.

In cases of cerebral and generalized arteriosclerosis, IODO-NIACIN has been used with great benefit[2]. Full doses were given for a year or longer without any iodism or ill effects.

The formula of IODO-NIACIN Tablets contains potassium iodide 135 mg. (2¼ gr.) combined with niacinamide hydroiodide 25 mg. (⅜ gr.). IODO-NIACIN Ampuls 5 cc. are highly satisfactory for intramuscular or intravenous use[3].

Since the retina is intrinsically a part of the brain[4], hemorrhages in this region are indicative of a similar cerebral condition for which IODO-NIACIN is directly indicated.

IODO-NIACIN Tablets, slosol coated pink, are supplied in bottles of 100. Ampuls 5 cc. in boxes of 10.

1. *Am. J. Ophth.* 42:771, 1956.
2. *Am. J. Digest Dis.* 22:5, 1955.
3. *Med. Times* 84:741, 1956.
4. *Cecil's Textbook of Medicine*, 7th ed., 1947, p. 1598.

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Gentlemen: Please send me professional literature and samples of IODO-NIACIN.
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STREET _____
CITY _____ STATE _____ ZONE _____

PROBLEM: How to be certain that your patients will properly take care of their contact lenses.

SOLUTION: Proper contact lens care and correct sanitary habits require that patients have the necessary solutions available at all times. The practitioner can be the source from which the patients are able to obtain these solutions. You can then be assured that they are practicing correct contact lens care, and enable your patients to continue the proper sanitary habits which you originally taught them.

We have available a complete inventory of solutions from the leading ophthalmic manufacturers. These solutions will provide complete sanitary care for your patient's contact lenses.

BARNES-HIND SOLUTIONS

WETTING AGENT
Provides complete sanitary wetting of contact lenses. Rapid cleaning action and ease of use will encourage proper sanitary care of contact lenses. Available in 5 cc. and 2-ounce polyethylene bottles.

SOAKING SOLUTION
A 4-ounce single-drop dispensing package that will provide cleaning action and maintain the wetting ability of contact lenses. Available in the 4-ounce polyethylene bottle.

TAMA® SOLUTIONS

WETTING SOLUTION
Effective cleansing solution provides complete hydration. The wetting activity is aided by the viscosity and spreading characteristics of this solution. Available in 5 cc. and 2-ounce polyethylene bottles.

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Effective cleanser provides sanitary overnight soaking. Aids in maintaining wetting ability and wearing comfort. Available in 5 cc, and 4-ounce polyethylene bottles.

CONTACTISOL SOLUTIONS

WETTING SOLUTION
Sterile packed wetting solution that will aid wearing comfort and assist your patients in increasing wearing time during the adaptive period. Available in 2-ounce and 7½ cc. polyethylene bottles.

SOAKING SOLUTION
An effective cleaning solution which aids in maintaining optical clarity of your patient's contact lenses. Available in 4-ounce and 7½ cc. polyethylene bottles.

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SUBNORMAL VISION AIDS VS. "CONTASCOPE" SPECTACLES

While the various types of subnormal vision aids available today perform satisfactorily for central vision, they are not generally accepted because of their limited field of vision and poor cosmetic value.

"Contascope" Spectacles consist of a minus power contact lens fitted conventionally, combined with a convex spectacle lens. The distance between the contact lens and spectacle lens is from 15 to 20 mm., forming a telescopic effect with a wide field of vision and any magnification desirable up to certain practical limits, the outside limit usually being 2 power.

The spectacle lens can be made in either single vision or bifocal form, giving the patient magnification for both distance and reading fields. The appearance is not objectionable, since the viewer merely sees spectacles carrying the equivalent of a cataract lens.

Here are two case histories we have fitted recently:

Vision unaided = 20/200

Refraction: +3.50 +1.75 × 90

Vision with regular spectacles = 20/100

"Contascope" Spectacles:

—11.00D contact lens

+ 10.50 + .50 × 15 spectacle lens fitted 20 mm. from cornea

+3.00 add

Result: 20/70 vision for distance and Jaeger 3.

Vision unaided = 20/140

Refraction: +1.25 —1.50 × 73

Vision with regular spectacles = 20/130

"Contascope" Spectacles:

—18.00D contact lens

+ 14.00 spherical bifocal lens fitted 22 mm. from cornea

+3.00 add

Result: 20/60 for distance and Jaeger 3.

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AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 49 JUNE, 1960 NUMBER 6

UVEITIS*

II. PERIPHERAL UVEITIS: CLINICAL DESCRIPTION, COMPLICATIONS AND DIFFERENTIAL DIAGNOSIS

R. J. BROCKHURST, M.D., C. L. SCHEPENS, M.D., AND I. D. OKAMURA, M.D.
Boston, Massachusetts

In recent years there has been a better opportunity to examine the extreme fundus periphery clinically as the result of the development of a binocular indirect ophthalmoscope[1] and the improvement in the technique of scleral indentation.[2] Although interest in the extreme fundus periphery was stimulated initially to obtain a better understanding of retinal detachment cases, it has become evident that many other types of ocular pathology occur in this area, either exclusively, or in an early stage before pathologic changes occur elsewhere in the eye. In 1950 Schepens,[2-4] described the findings in 38 patients with a form of uveitis in which the earliest pathologic changes occur in the extreme fundus periphery. For this reason, he called this condition "peripheral uveitis." The present paper is a more complete report based on the observation of 100 patients, nine of whom were previously studied by Schepens. Of the 100 patients herein reported, 48 were female, 52 were male. A total of 175 eyes were involved, as 75 patients showed peripheral uveitis in both eyes during the follow-up period which ranged from one to eight years.

This report includes a clinical description of peripheral uveitis, which is subdivided into a discussion of its symptoms, the earliest changes observed in the fundus periphery and anterior chamber angle, and the different courses which the disease may take. Complications and differential diagnosis are discussed and followed by comments. A subsequent paper will deal with the pathogenesis, etiology, and treatment of peripheral uveitis.

CLINICAL DESCRIPTION

SYMPTOMS

Three patients had active peripheral uveitis without symptoms, and the presence of peripheral uveitis was discovered as the result of a complete ocular examination performed, for example, because of high myopia, in the course of a survey of relatives of patients with detached retinas, or during examination of apparently normal eyes for a control series. In these instances the patients denied any history of ocular difficulty. Forty-one patients complained of mild symptoms such as seeing black spots, strands, thin veils, or having blurred vision. Some patients related that the affected eye became slightly red, and at times an aching or tired sensation was noted. It is apparent that these symptoms are not very specific. In severe cases there may be serious loss of vision, both central and peripheral as a consequence of fundus changes. Fifty-six patients fell in this group. Table 1 summarizes the nature and incidence of symptoms observed.

* From the Retina Foundation, Department of Ophthalmology, Massachusetts Eye and Ear Infirmary and Harvard Medical School. (Paper No. 62, Retina Foundation.) This work was supported by Grant No. B633 of the Institute of Neurological Diseases and Blindness, National Institutes of Health, Department of Health, Education and Welfare, Bethesda, Maryland.

TABLE 1

SYMPTOMS OF PERIPHERAL UVEITIS

Symptoms	Number of Patients
None	3
Mild: black spots, veils, slight blurring of vision, asthenopia	41
Severe: serious loss of central and/or peripheral vision	56
TOTAL	100

EARLY CHANGES

In the early stages of the disease, fundus changes may be limited to a few aggregates of exudative material in the vicinity of the ora serrata. Yellowish gray globular exudates may be found on the pars plana ciliaris, at the ora serrata, or on the anterior portion of the retina. These exudates are often, but not invariably, associated with signs of periphlebitis of the terminal branches of the retinal venules as evidenced by sheathing, obliteration, and exudation along the vessels (fig. 1). Rarely the terminal arterioles show similar changes. As the process continues, the exudative globules may coalesce to form a massive plaque which covers the ora serrata region, hiding all normal landmarks in that region (fig. 2). For some unexplained reason, peripheral exudates are nearly always more numerous and more extensive in the lower half of the fundus.

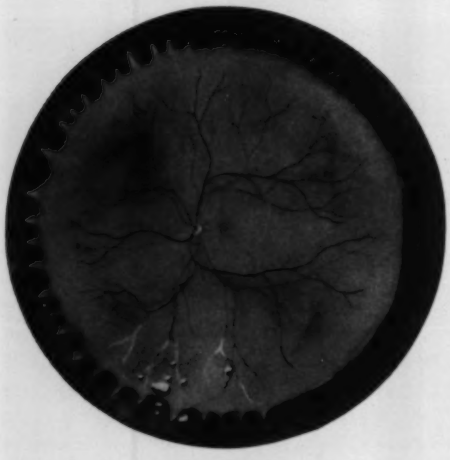

Fig. 1 (Brockhurst, Schepens and Okamura). Early stage of peripheral uveitis, showing mild periphlebitis of retinal venules near the ora serrata, small gelatinous exudates along these vessels, and early exudation in the pars plana ciliaris.

Fig. 2 (Brockhurst, Schepens and Okamura). Later stage of peripheral uveitis with development of a massive exudate which obscures normal landmarks of the extreme fundus periphery. Note also the small exudates lying on the retina.

In addition, exudative material may break loose, either from this mass, or from the perivascular area, and enter the vitreous cavity. Exudates in the vitreous cavity generally have the appearance of white or yellowish "cotton balls" which lie close to the retina. The macula often shows edema, and in time may develop pigmentary degeneration.

In 21 patients gonioscopic examination showed gelatinous yellowish gray exudates on the trabeculae. In a previous report[3] we have noted their resemblance to mutton-fat keratic precipitates, and their role in the formation of peripheral anterior synechias as a result of adhesions between the iris and trabecular exudates. It is noteworthy that these exudates may be present in the absence of keratic precipitates, and may be found in all quadrants of the angle (fig. 3).

In summary, the early stage of the disease

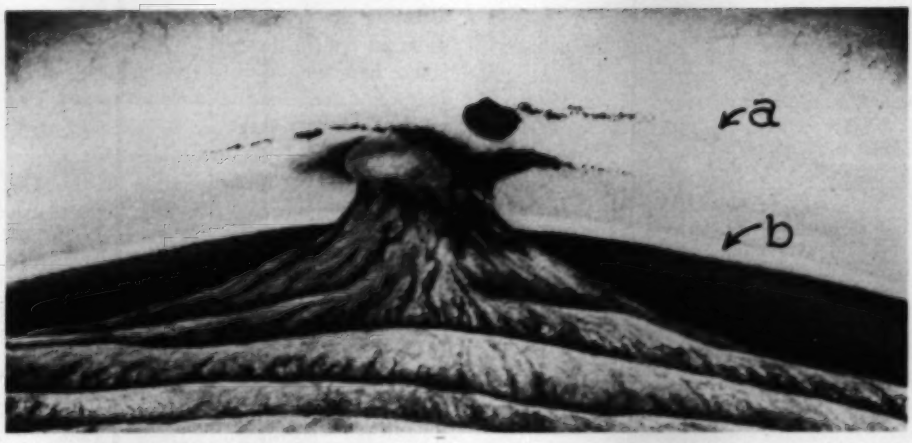

Fig. 3 (Brockhurst, Schepens and Okamura). This exudate, on the trabeculae of the angle, has caused an iris-exudate adhesion. It is the forerunner of a peripheral anterior synechia. (a) Schwalbe's line (b) Scleral spur.

is characterized by exudative material in the extreme fundus periphery, which may be associated with exudates in the filtration angle.

Course

Later, the inflammatory process may: (1) remain benign and subside, (2) lead to choroidal detachment which may be accompanied by retinal detachment without retinal breaks, (3) result in the development of a cyclitic membrane, (4) precede a progressive occlusion of the retinal vessels, and (5) smolder on in a chronic form for many years. Table 2 summarizes the number, sex, and ages of patients which followed these different courses.

In 28 patients the course of the inflammatory disease was benign. In some instances the process cleared entirely, all exudative material in the fundus periphery and in the chamber angle disappearing after a few months. In others only slight atrophy of the choroid or pars plana ciliaris was noted. The only result of previous trabecular precipitates in this type of case were a few trabecular peripheral anterior synechias. Some cases showed, as a residual finding, a flat retinal detachment without retinal breaks, in the vicinity of the ora serrata (fig. 4). It is possible that peripheral retinal breaks, which are found adjacent to obliterated retinal blood vessels, are the result of a peripheral uveitis. To date this sequence of events has not been observed. However, in one patient, referred

TABLE 2

Course of peripheral uveitis

Type of Course	Number of Patients			Age		
	Male	Female	Total	Under 30 Yr.	Over 30 Yr.	Median Age (yr.)
1. Benign	8	20	28	14	14	30
2. Secondary choroidal and/or retinal detachment without breaks	10	2	12	1	11	51
3. Cyclitic membrane	4	2	6	6	0	9
4. Vascular occlusion	6	2	8	2	6	36
5. Chronic, smoldering	24	22	46	21	25	32

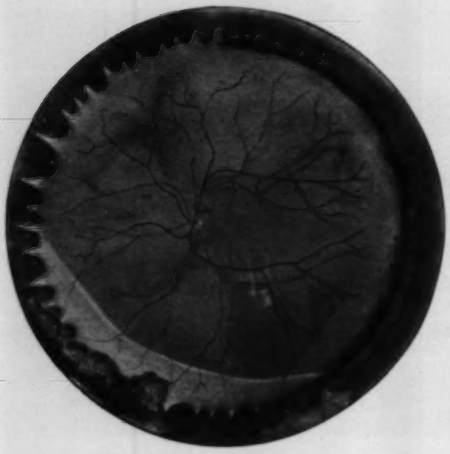

Fig. 4 (Brockhurst, Schepens and Okamura). Sequelae of mild peripheral uveitis: areas of chorioretinal atrophy and flat subclinical retinal detachment without retinal breaks.

because of retinal detachment, peripheral retinal breaks were associated with retinal periphlebitis and active exudation in the region of the pars plana ciliaris and ora serrata.

In 12 patients, 11 of whom were over 30 years of age, there was predominantly an annular involvement of the pars plana ciliaris and of the peripheral portion of the choroid. It is of interest that 10 of the patients were males. The chief finding was a peripheral choroidal detachment in all quadrants (fig. 5). Exudates near the ora serrata and sheathing of the terminal vessels of the retina were usually present. In most cases there was a secondary retinal detachment without retinal breaks, which must be differentiated from idiopathic retinal detachment. Any retinal detachment operation which was performed on this type of secondary retinal detachment with peripheral uveitis has usually made the condition worse. In six patients where no surgery was performed, the inflammatory process subsided after several months of steroid therapy, 30 to 40 mg. of prednisone per day, with reattachment of the retina and return of vision. Patients having this disorder in one eye often have a similar process affecting the fellow eye either concurrently or from one to three years later. In no instance have we observed the development of features to suggest Harada's disease, such as marked vitreous haze, severe choroidal atrophy, vitiligo, poliosis, alopecia, and dysacousia. We feel that the recognition of this disorder is so important that a subsequent report will be devoted to this type of peripheral uveitis.

In six patients a malignant progressive form of peripheral uveitis was observed. All patients were 15 years of age or less. This type was characterized by the development of a massive yellowish gray exudate overlying the ora serrata region. Then gradually over a period of several months an insidious vascularization of this massive exudate occurred, the new vessels originating from the ciliary body and not from the retina (fig. 6). The new-formed vessels were first seen in the anterior portions of the exudate from which they extended posteriorly. This development was most often observed inferiorly between the 3- and 9-o'clock positions. At this stage,

Fig. 5 (Brockhurst, Schepens and Okamura). Peripheral uveitis with choroidal detachment in four quadrants, total secondary retinal detachment without retinal breaks, and two exudates in the pars plana ciliaris, at the 6- and 7-o'clock positions. Ciliaris processes are visible in three quadrants as a result of the choroidal detachment.

Fig. 6 (Brockhurst, Schepens and Okamura). Massive peripheral exudate with neovascularization from the ciliary body; this is the early stage of a cyclitic membrane. There is an inferior retinal detachment due to traction (no retinal breaks were found). Note the periphlebitis of peripheral retinal venules.

the fundus appearance often simulated an intraocular new growth. As the process continued, the vascularized exudate involved the equatorial region of the lens and proliferated on the posterior capsule forming a cyclitic membrane (fig. 7). Associated with the development of this membrane posterior cortical lens opacities began to appear and vitreous opacities increased. In the later stages the retina was pulled off by the cicatrizing membrane adherent to the retinal periphery (fig. 8). With further cicatrization, the lens-iris diaphragm moved forward and secondary glaucoma ensued.

A chronic form of peripheral uveitis, associated with vascular changes in the posterior fundus, was observed in eight cases. Initially the peripheral uveitis with exudative changes near the ora serrata was associated with marked sheathing and periphlebitis of the terminal veins. Gradually the sheathing of the veins progressed posteriorly toward the disc. In some cases, the sheathing was so dense that the blood column could not be visualized in some sections of the veins. In time the veins became obliterated, and resulting retinitis proliferans was not rare. Secondary retinal degeneration and pigmentation followed with loss of visual field and central vision. In their terminal stage such cases showed optic atrophy and obliteration of the arterioles (fig. 9); clinically indistinguishable from an obstruction of the central retinal vessels. The essential difference was that, in the cases described, the process started in the periphery of the fundus, not in the region of the disc.

Fig. 7 (Brockhurst, Schepens and Okamura). Later stage of a cyclitic membrane as seen through the pupil.

In 46 cases a chronic, smoldering process

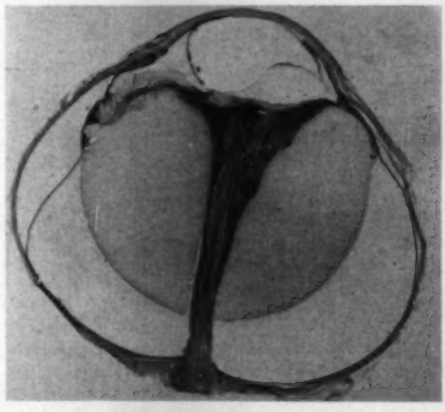

Fig. 8 (Brockhurst, Schepens and Okamura). Histologic section showing total retinal detachment due to cicatrizing cyclitic membrane. (R.S. #766.)

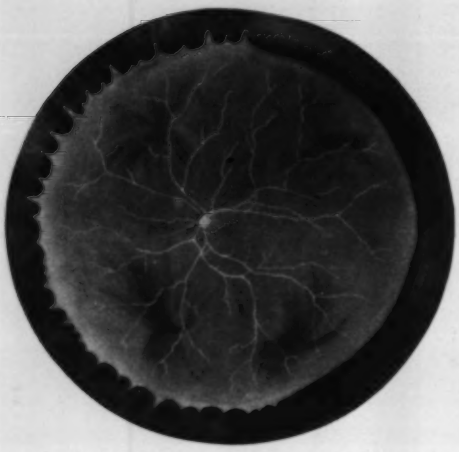

Fig. 9 (Brockhurst, Schepens and Okamura). Progressive obliteration of retinal vessels following peripheral uveitis, accompanied by optic atrophy.

was observed with minor exacerbations and remissions going on for years. The result was that some areas of the fundus periphery exhibited active exudates while others showed quiescent peripheral chorioretinitis (fig. 10). In cases where a gelatinous massive exudate was observed overlying the fundus periphery, it cicatrized forming a limited membrane located in the vitreous cavity and which obscured the ora serrata region. This membrane was either gray and translucent or chalk white. In some instances, holes developed in the membrane (fig. 11). In one patient the membrane had been erroneously interpreted as a detached retina and the holes in the membrane as retinal breaks. The formation of holes in a new-formed membrane has been observed to result from a pincer type arrangement of the active exudates (fig. 12). This type of membrane has caused a true retinal detachment by the traction it exerted on the equatorial portion of the retina under the membrane. Slitlamp examination of the vitreous body often showed dense irregular membranes which were adherent to the posterior lens capsule. As the process continued, posterior cortical opacities began to appear in the lens adjacent to these vitreolental adhesions. The ultimate fate of most of the eyes showing this low-grade chronic form of peripheral uveitis cannot as yet be stated with certainty, since the follow-up

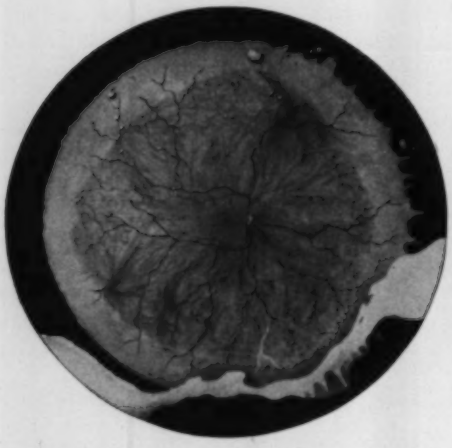

Fig. 10 (Brockhurst, Schepens and Okamura). Chronic, smoldering form of peripheral uveitis. In the lower temporal periphery active exudates are present; whereas in the lower nasal periphery cicatrization with membrane formation has occurred. Scattered exudates with periphlebitis of peripheral retinal venules are also present.

Fig. 11 (Brockhurst, Schepens and Okamura). Chronic, smoldering form of peripheral uveitis. Cicatricial membrane with hole lies slightly internal to the retina in the vitreous cavity. Such a membrane may be mistaken for a retinal detachment.

period in most instances is less than eight years. It is apparent, however, that visual loss may be caused by secondary macular degeneration, posterior cortical cataract, membrane formation in the vitreous and retinal detachment. Secondary glaucoma may be caused by the progressive formation of peripheral anterior synechias.

Complications

The complications of peripheral uveitis include band keratopathy, peripheral anterior synechias, posterior synechias, glaucoma, posterior cortical cataract, vitreous hemorrhage, macular edema and degeneration, and retinal detachment either due to retinal breaks or to traction on the retina without demonstrable breaks. Table 3 summarizes the incidence of these complications observed in the various types of peripheral uveitis encountered.

Band keratopathy was found in three of 100 patients, all young females aged seven to nine, none of whom suffered from arthritis. These patients had the chronic, smoldering form of uveitis and suffered severe loss of vision.

Peripheral anterior synechias were noted in 24 of 100 patients. Eighteen showed both angle exudates and peripheral synechias, and in four cases the peripheral anterior synechias were observed to form as a result of these exudates.[3] Posterior synechias were present in 18 patients, 13 of whom had the chronic form of peripheral uveitis. In regard to synechia formation, it is of interest that peripheral anterior synechias formed in 10 of 28 patients (36 percent) affected by a type of peripheral uveitis which cleared up. On the other hand, posterior synechias formed in only two of the same group of 28 patients (seven percent). Thus, eyes which have previously had peripheral uveitis may fail to show posterior synechias, but gonioscopy may well reveal peripheral anterior synechias as a residual finding.

Glaucoma was present in 16 of 100 patients. In two patients severe angle-closure glaucoma developed. In one case the angle became closed as a consequence of an extensive choroidal detachment; in the other, it resulted from a swollen cataractous lens. In

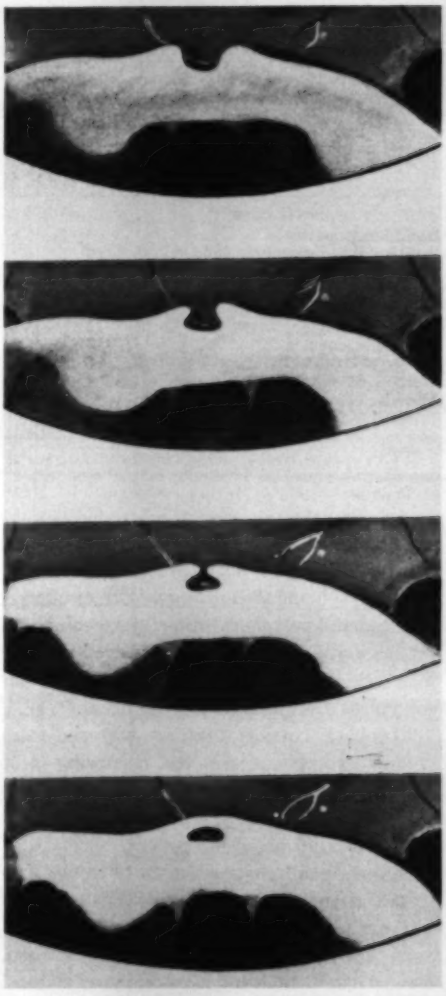

Fig. 12 (Brockhurst, Schepens and Okamura). Chronic, smoldering form of peripheral uveitis. Stages of formation of a hole in a cicatricial preretinal membrane located at the ora serrata. Active exudates build up prominences which coalesce. When the exudates subside, the membrane shows the appearance of a hole in it. Note the periphlebitis of retinal venules and the tiny retinal exudates near them.

TABLE 3

COMPLICATIONS OF PERIPHERAL UVEITIS

Complication	*Type 1* Benign Uveitis (28 Cases)	*Type 2* Secondary Choroidal and/or Retinal Detachment (12 Cases)	*Type 3* Cyclitic Membrane (6 Cases)	*Type 4* Vascular Occlusion (8 Cases)	*Type 5* Chronic, Smoldering Uveitis (46 Cases)	Total
Band keratopathy					3	3
Peripheral anterior synechias	10	1			13	24
Posterior synechias	2		3		13	18
Glaucoma:						
1. Angle-closure		1	1			2
2. Open-angle	2	1			5	8
3. Secondary	3		1	1	1	6
Posterior cortical cataract	8	4	2	3	19	36
Vitreous hemorrhage	1			1	1	3
Macular edema and/or degeneration	3		1	3	14	21
Idiopathic retinal detachment*	5	1	4	3	9	22

* This means retinal detachment due to retinal breaks or to traction by vitreous membranes without demonstrable breaks. It should not be confused with the secondary retinal detachment observed in cases of Type 2.

eight patients the glaucoma was of a chronic nature, significant portions of the filtration meshwork being compromised by exudative material and peripheral anterior synechias. In six instances the glaucoma appeared to be of the "secondary" type, subsiding with the control of the inflammatory process.

Posterior cortical cataract was the most frequent complication noted, occurring in 36 of 100 patients. In many cases the visual loss suffered by the patient was wholly attributable to the cataract development.

Severe hemorrhage into the vitreous cavity was seen in only three of 100 patients. Of interest is the fact that one young woman, aged 18 years, suffered a severe vitreous hemorrhage which for over one year reduced her vision to hand movements. This hemorrhage occurred in an eye with mild peripheral uveitis which later subsided. The hemorrhage cleared gradually and spontaneously with return of 20/20 visual acuity.

A serious visual loss occurred in 21 of 100 patients, as a consequence of macular edema and subsequent pigmentation and degeneration. This complication was most frequent in the chronic, smoldering type of uveitis, and in many of these cases, the initial diagnosis had been macular edema or macular degeneration. The primary cause of the macular disturbance was the uveitis in the extreme fundus periphery. This was discovered only after a careful ophthalmoscopic examination. It is, therefore, important to suspect a process of peripheral uveitis in patients with unexplained macular edema or macular degenerative changes.

Detachment of the retina was observed in 22 of 100 patients. This complication was the result of retinal breaks occurring in areas either of peripheral uveitis, or of traction by vitreous membranes resulting from uveitis. This complication is not to be confused with the type of peripheral uveitis in which a secondary choroidal and retinal detachment are produced by the inflammation itself.

DIFFERENTIAL DIAGNOSIS

From this description of the course and complications of peripheral uveitis, it is apparent that erroneous diagnoses may easily be made in patients with this disease. In order to avoid an error in diagnosis, it is necessary to study the extreme fundus periphery and the angle of the anterior chamber.

In patients who show loss of central vision with degeneration or edema of the macula, a

diagnosis of macular degeneration might be made when actually the macular lesions are secondary to a peripheral uveitis. Similarly cataractous changes, especially posterior cortical lens opacities, should always make the examiner suspect peripheral uveitis. All patients who exhibit an elevation of intraocular pressure should be gonioscoped, and if peripheral anterior synechias are found, peripheral uveitis should be suspected. If actual exudates are found on the trabeculae, the glaucoma usually is secondary to the uveitic process.

Peripheral uveitis should be considered as a possible cause of spontaneous choroidal detachment when the patient has not undergone intraocular surgery recently and has not suffered an ocular trauma. This type of choroidal detachment may be accompanied by a secondary retinal detachment in which the following characteristics are observed. The subretinal fluid shows a marked tendency to shift under the retina, the retina is usually attached near the ora serrata, and retinal breaks are absent. When a patient is seen with a retinal detachment showing such characteristics, the probability of a secondary detachment is great, and the cause may be peripheral uveitis.

Spontaneous vitreous hemorrhages may be caused by peripheral uveitis. Other types of vitreous opacities and membranes may also result from peripheral uveitis and are not necessarily a consequence of degenerative changes in the vitreous body. It is imperative that in the presence of unexplained vitreous membranes and opacities, a careful examination of the fundus be performed, including the extreme periphery. Gray membranes in the vitreous, overlying the peripheral retina, may be interpreted as a retinal detachment if the extreme fundus periphery is not carefully examined with scleral indentation. The following signs help the examiner to rule out retinal detachment: a translucent vitreous membrane which is avascular, located near areas of choroidal atrophy; the presence of exudates in the fundus periphery. Retinoschisis[5] might be confused with such membranes, but the thin internal layer of the retinoschisis shows either patent or obliterated retinal vessels and tiny gray dotlike deposits. It usually extends around the entire fundus periphery and is practically always bilateral.

The finding of vascular disease in the retinal vessels always poses a problem as to etiology and differential diagnosis. It is apparent that in patients who exhibit sheathing and obliteration of the central retinal veins, more marked in the distal branches, the probability is great that peripheral uveitis is the primary disorder. In such patients the optic nervehead gradually becomes pale and atrophic, and the retinal arterioles become attenuated and obliterated; thus the association of optic atrophy with vascular disease of the peripheral retina suggests the existence of peripheral uveitis.

Finally the presence of an organizing membrane behind the lens, suggestive of disorders like retrolental fibroplasia, vitreous hyperplasia, and intraocular tumor, also suggests the possibility of an active and severe peripheral uveitis, especially if the patient is a child.

Comment

Peripheral uveitis is to be classified as a granulomatous type of uveitis because it is manifested by gelatinous type exudates in the anterior chamber angle and in the fundus periphery. It has a chronic course, and leads to organic changes. With the usual methods of investigation, such as direct ophthalmoscopy and slitlamp examination, most of these cases would be classified as nongranulomatous uveitis. In our opinion many cases which appear to be nongranulomatous uveitis, by the usual methods of examination, actually show granulomatous changes either in the anterior chamber angle or in the extreme fundus periphery.

Chorioretinitic lesions posterior to the equator were seen in 24 of 100 patients with peripheral uveitis. Because of this finding, these patients would ordinarily be labeled as

having granulomatous uveitis. The other 76 patients showed granulomatous foci in the anterior chamber angle or the extreme fundus periphery without granulomatous foci posterior to the fundus equator.

Peripheral uveitis should be suspected in all patients showing one or more of the following signs for no obvious reason: flare or cells in the anterior chamber, peripheral anterior synechias, vitreous opacities, posterior cortical cataract, macular edema and degeneration, choroidal detachment, and retinal detachment without retinal breaks.

Summary

Peripheral uveitis is a type of granulomatous uveitis wherein the earliest clinical changes are found in the extreme fundus periphery and the anterior chamber angle. This paper describes findings observed in 100 patients with this disorder. In the early stage one may observe gelatinous exudates in the region of the ora serrata and pars plana ciliaris, particularly below, similar exudates on the trabeculae of the anterior chamber angle, and vascular sheathing of the terminal retinal vessels. At a later stage, the disorder may follow one of five courses: (1) benign type which gradually subsides; (2) development of choroidal and retinal detachment without retinal breaks; (3) malignant course with development of a cyclitic membrane and detachment of the retina by organizing membranes in the vitreous cavity; (4) progressive occlusion of the retinal veins beginning in the periphery and extending toward the disc with ultimate optic atrophy; and (5) chronic smoldering form. In many cases complications may occur such as peripheral anterior synechias, glaucoma, posterior synechias, posterior cortical cataract, macular degeneration, retinal degeneration and retinal breaks followed by idiopathic retinal detachment.

Of 100 patients studied, 76 showed no granulomatous foci posterior to the equator, although such foci were found either in the anterior chamber angle or in the extreme fundus periphery. It is apparent that many cases which appear to have nongranulomatous uveitis by the usual methods of examination, such as biomicroscopy and direct ophthalmoscopy, actually show evidence of granulomatous disease by indirect stereoscopic ophthalmoscopy with scleral indentation and gonioscopy.

99 West Cedar Street (14).

Acknowledgment

Drawings in this paper were done by Mr. William J. Stenstrom.

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AN UNKNOWN CANALICULAR NETWORK OF THE IRIS REVEALED BY MICRORADIOGRAPHY*

J. François, M.D., A. Neetens, M.D. and J. M. Collette, M.D.
Ghent, Belgium

The importance of the iridocorneal angle in the outflow of aqueous humor cannot be denied; experimentally, it is sufficient to recall that in vitro perfusion of the anterior chamber under physiologic pressure reveals the almost instantaneous appearance of fluid at the level of the limbus.

Yet there remain certain problems so far unsolved, and it is with one of these that this paper will be concerned.

In order to prevent the fluid introduced into the anterior chamber and flowing through the trabecular meshwork and Schlemm's canal, from penetrating the intrascleral vessels, the least trace of conjunctiva and episcleral tissue is removed from the eyeball, after which a lamellar and annular scleral resection is made round the limbus, removing a width of about three to four mm. and going almost as deep as the canal of Schlemm, which is marked by means of a previous injection of methylene blue.

The eyes thus prepared are then perfused for 10 minutes with Thorotrast, introduced into the anterior chamber under physiologic pressure.

The iris is then submitted to microradiographic examination which reveals, apart from irregular superficial spots due to impregnation of the anterior surface and the crypts of the iris, an unknown canalicular network localized in the mesodermal layer of the iris and consisting of two parts, namely, a peripupillary part, with radial marks, and a peripheral part with circular marks (fig. 1).

The radial marks are parallel but of irregular width. On the pupillary side they pass the mesodermal tissue of the iris, ending either in a loop joining the next mark or in a point which unites two radial marks (figs. 2A, 2B, and 3).

In the median part of the iris these marks are connected by circular marks (intermediary zone between the peripupillary and the peripheral part); or they may end here in an annular or oval formation, complete or incomplete, within which no Thorotrast is visible (fig. 4).

A circular structure predominates in the peripheral part of the iris; the still-parallel marks, close together and undulating, form a circular network interrupted by incontinuous radial marks at more or less regular intervals; the circular marks seem to converge toward the radial marks, describing a concave line towards the interior (fig. 5).

This regular network, completely different from the vascular network of the iris and seemingly canalicular, is found in all normal young irises.

We have been unable to demonstrate it, however, when the anterior chamber was perfused under considerable pressure (for example, 100 cm. water).

On the other hand, the same network appears when the iris is isolated and simply placed in Thorotrast, then washed in physiologic saline and fixed; this indicates that filling is instantaneous and based on capillarity.

The same network is seen when the experiment is carried out with an iris deprived of its pigmentary layer; the network must therefore be localized in or at the level of the mesodermal layer of the iris.

Concerning microradiography of the ciliary body and the pars plana in the course of these Thorotrast perfusion experiments, the following can be said:

Apart from impregnation features, which constitute a fine replica of the contorted sur-

* From the Ophthalmological Clinic of the University of Ghent (Prof. J. François) and from the Radiological Laboratory of the University of Liège (Prof. G. Leroux).

Fig. 1 (François, Neetens and Collette). General survey of the canalicular network of the iris and impregnation image of the ciliary processes (×18.5). Injection of Thorotrast into the anterior chamber under physiologic pressure.

face of the ciliary processes, more interesting features can be obtained by removing the ciliary processes (fig. 1). No vessels are then visible but a more or less regular shadow is seen, which extends toward the pars plana in always doubled markings, between which a discrete shadow reveals the perivascular Thorotrast (figs. 6A and 6B).

At the level of the pars plana, but more markedly so at the level of the choroid, a truly vascular structure subsequently appears in the midst of the perivascular shadows (fig. 7, 8, and 9).

These images point to the possibility of flow to a certain extent.

The question arises as to whether there are small apertures in the anterior surface of the iris, at which sites the endothelium is lacking and which may constitute the mouths of the canalicular network. Zimmerman (Armed Forces Institute of Pathology, Washington) examined sections of human iris stained according to Wilder, and saw an apparent discontinuity in the cellular anterior layer, with an accumulation of reticulin fibrillae at the sites of the interruptions (figs. 10, 11, 12, 13, and 14).

Fine and Tousimis, of the Armed Forces Institute, furnished electron-microscopic evidence that the anterior surface of the iris does not form a continuous layer but one with numerous apertures, at the sites of which there are fibrillae with a periodicity characteristic of collagen (640 Å) (fig. 15).

Gregersen (1958) carried out in vivo perfusion of human eyes, using a dextrose solution, and performing enucleation six to 15 minutes later. Histologic examination of such irises showed dextrose not only in the

(Text continued on page 1277)

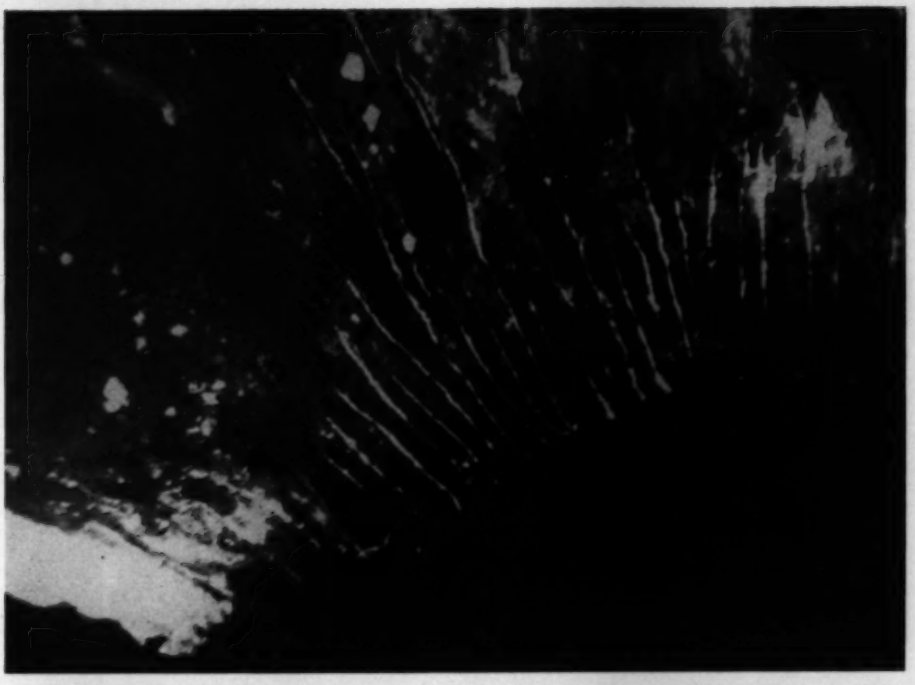


Fig. 2A (François, Neetens and Collette). The canalicular iris network at the pupillary border (×52.5).

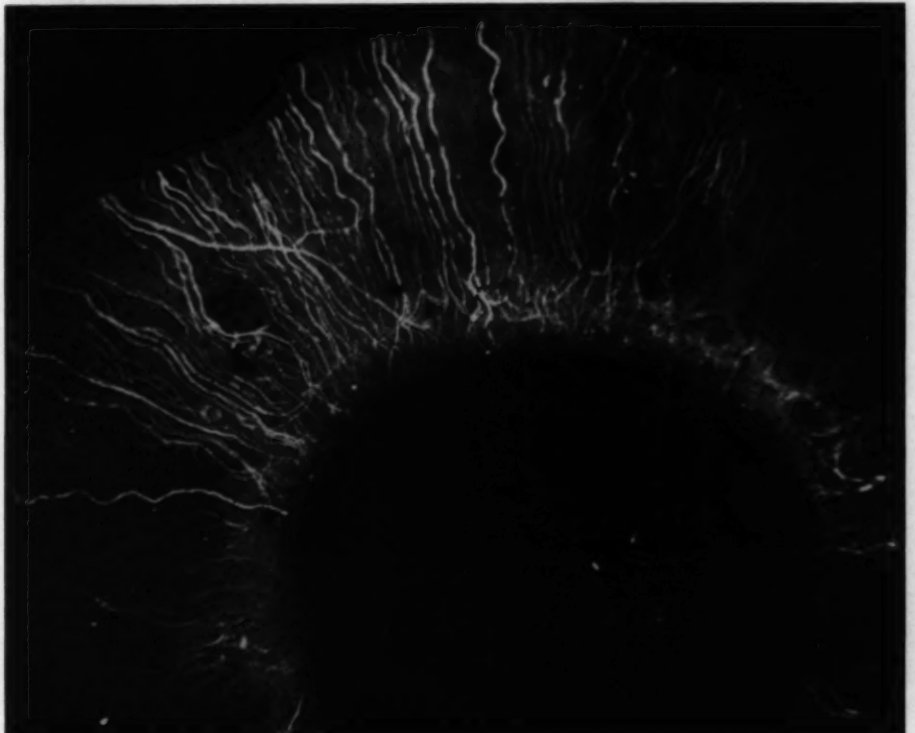


Fig. 2B (François, Neetens, and Collette). Comparative normal vascularization of the iris (×19.5).

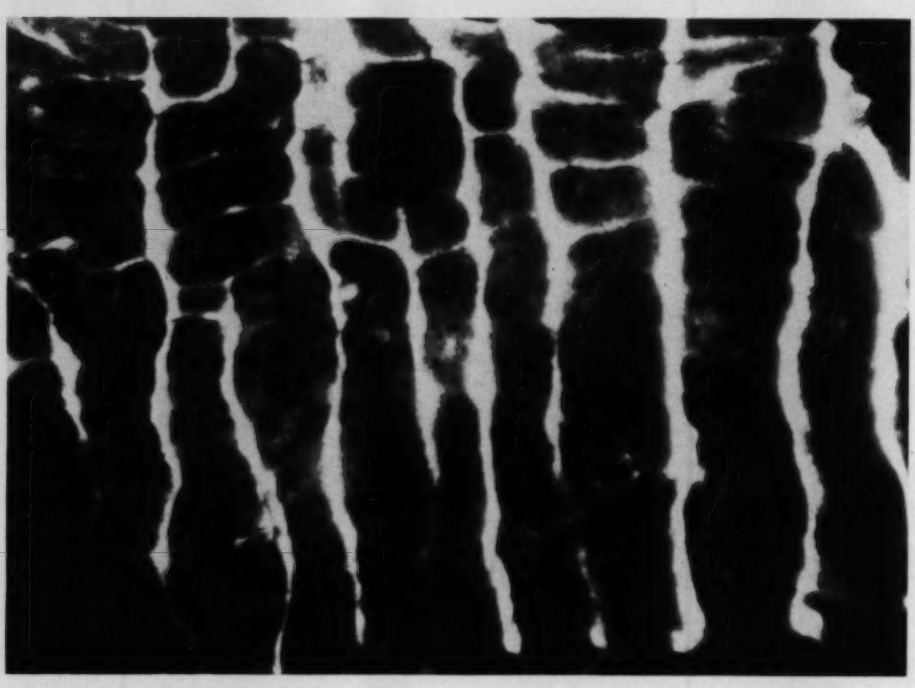


Fig. 3 (François, Neetens and Collette). Transitional zone between the pupillary area and the area at the base of the iris (×195).

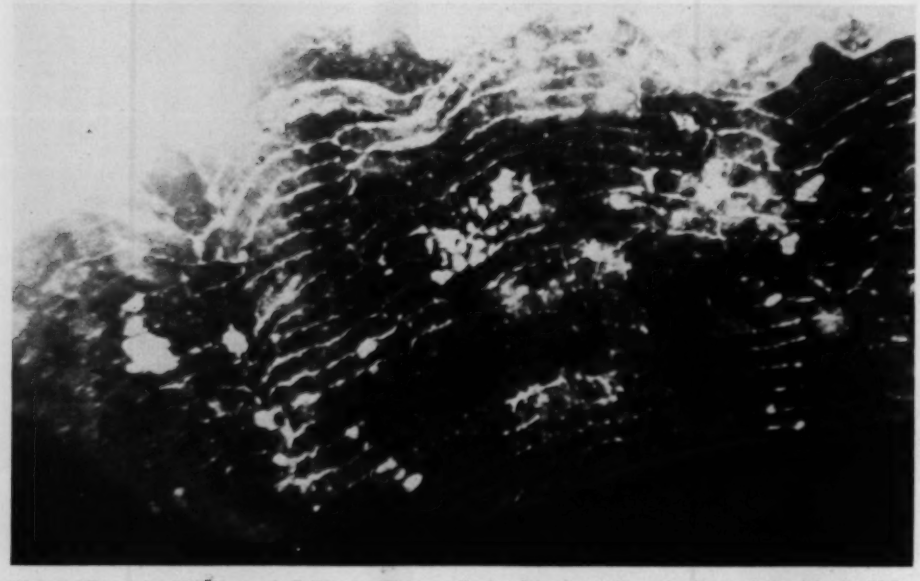


Fig. 4 (François, Neetens and Collette). The canalicular iris network at the base of the iris (×52.5).

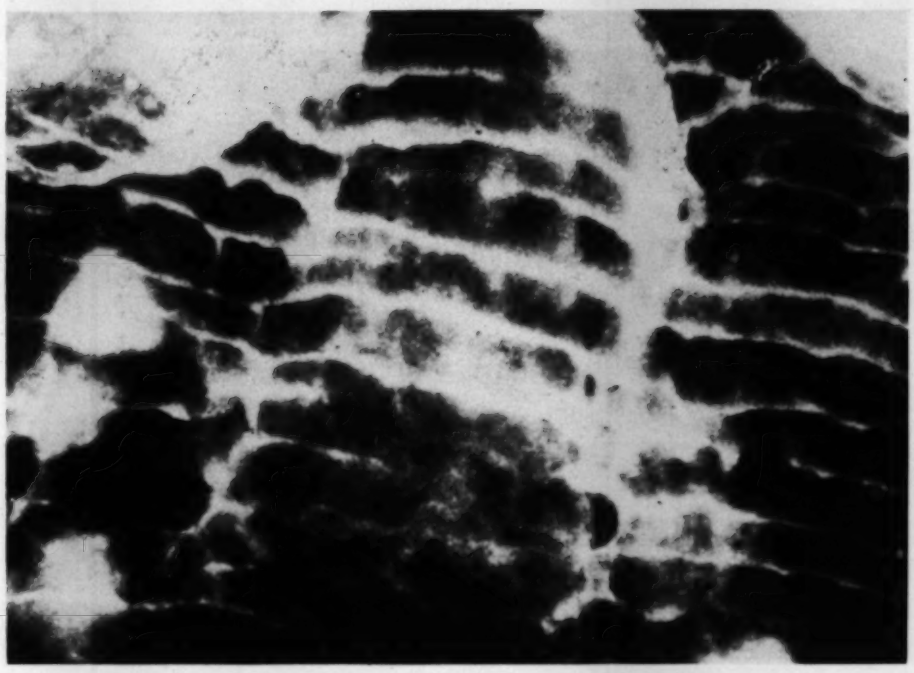


Fig. 5 (François, Neetens and Collette). The same network as in Figure 4 (×195).

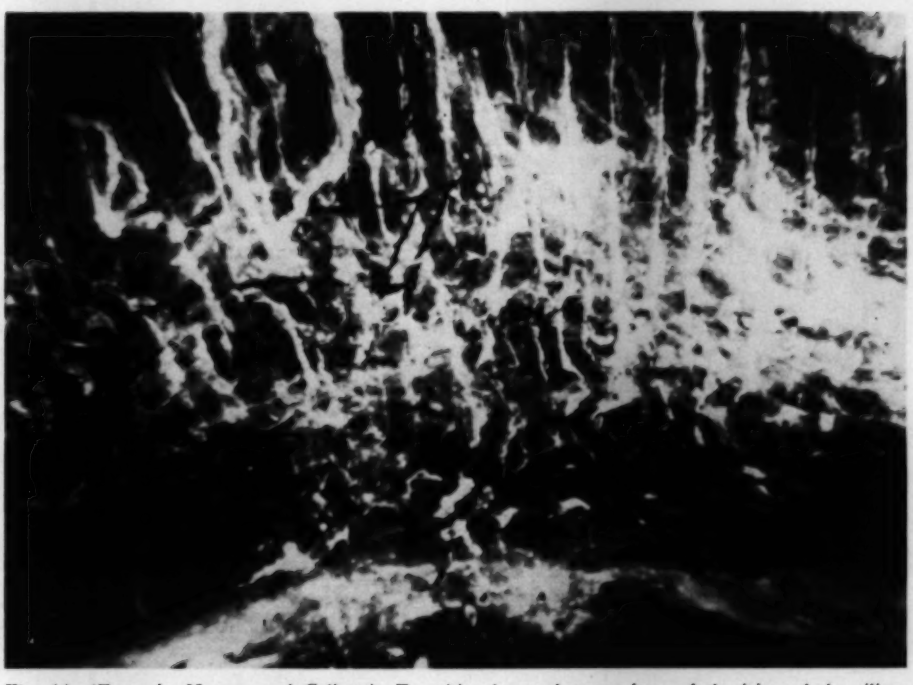


Fig. 6A (François, Neetens and Collette). Transitional zone between base of the iris and the ciliary body (×52.5). As much of the ciliary processes as possible were dissected away.

Fig. 6B (François, Neetens and Collette). Comparative image of the vascularization of the ciliary body and the choroid (×19.5).

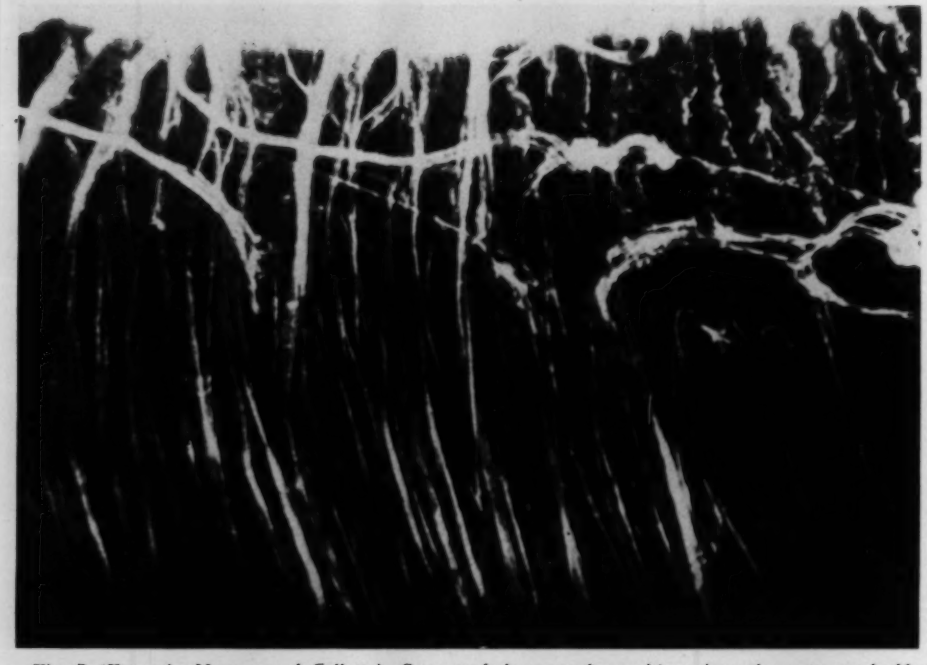


Fig. 7 (François, Neetens and Collette). Survey of the pars plana with perivascular pattern; double outlining with large and narrower interstitial spaces, alternating regularly and showing the flow gradient.

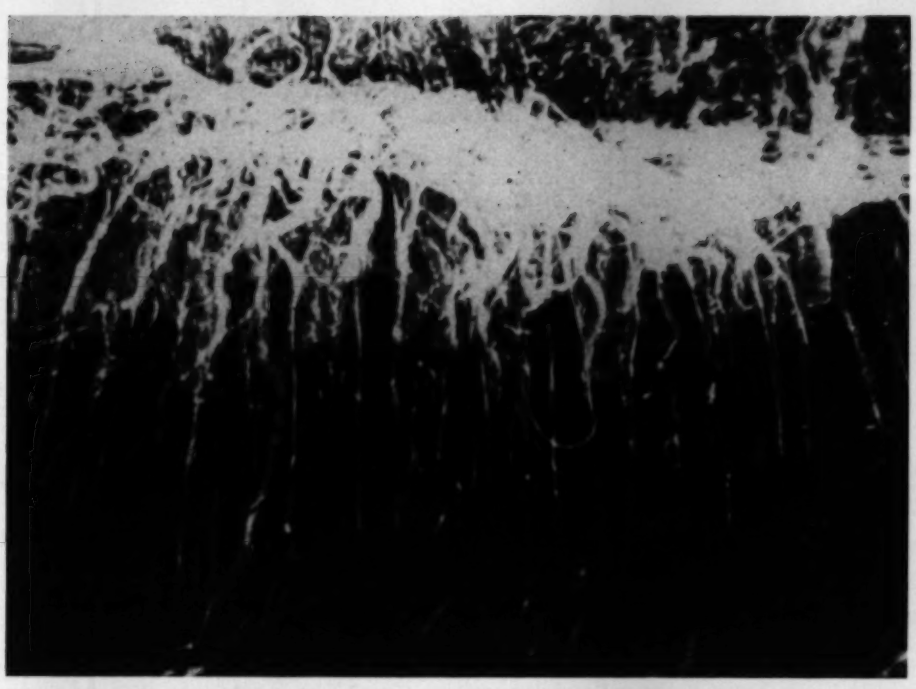


Fig. 8 (François, Neetens and Collette). Here and there, real vascular images appear. Are they the possible diffusion from the perivascular spaces to the vessel itself? (×52.5)

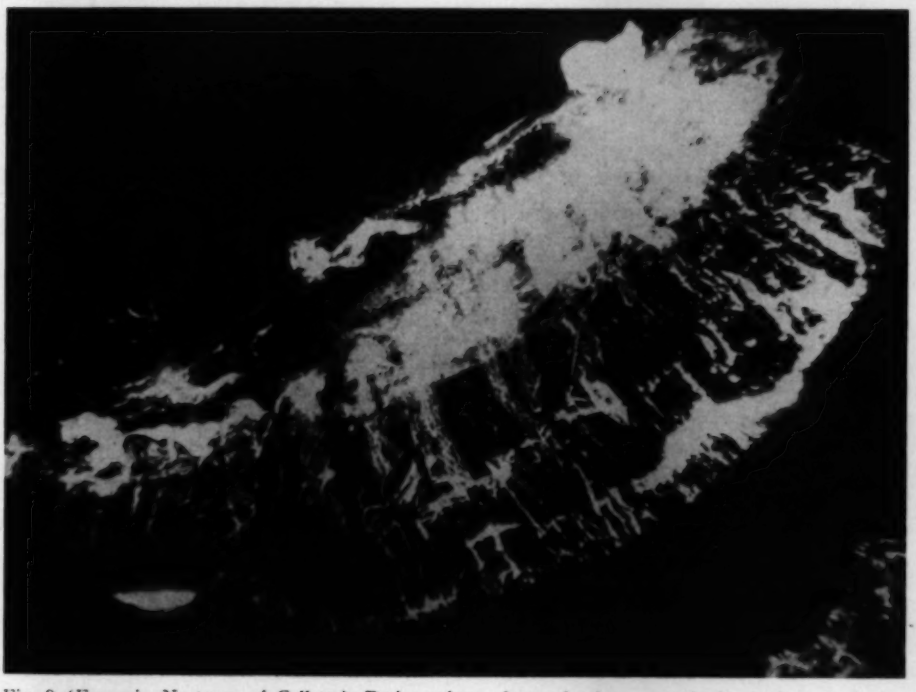


Fig. 9 (François, Neetens and Collette). Perivascular and vascular images at the level of the beginning choroid itself (×19.5).

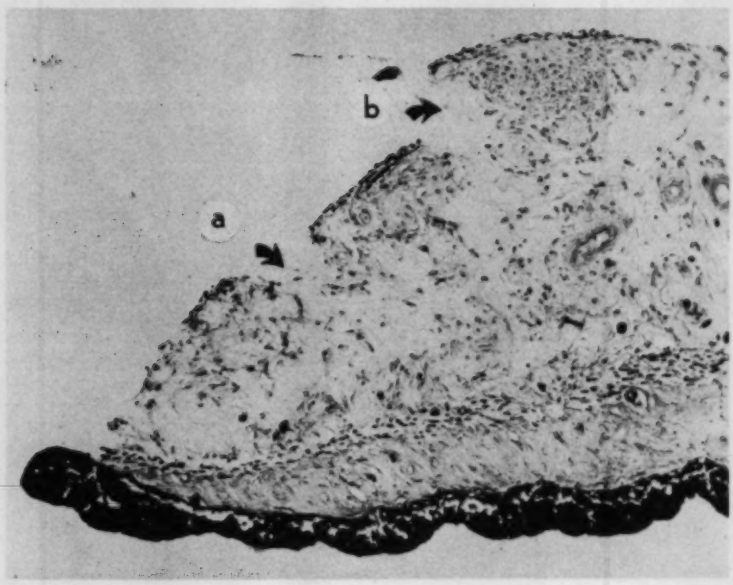


Fig. 10 (François, Neetens and Collette). Two areas where the anterior border cells do not form a continuous membrane enclosing the iris stroma are indicated by arrows (a) and (b). Area (a) is shown at higher magnification in Figure 11. (Wilder reticulum stain, ×112.) (Courtesy of Lorenz E. Zimmerman, M. D., Department of Ophthalmic Pathology, Armed Forces Institute of Pathology, Walter Reed Medical Center, Washington 25, D.C.)

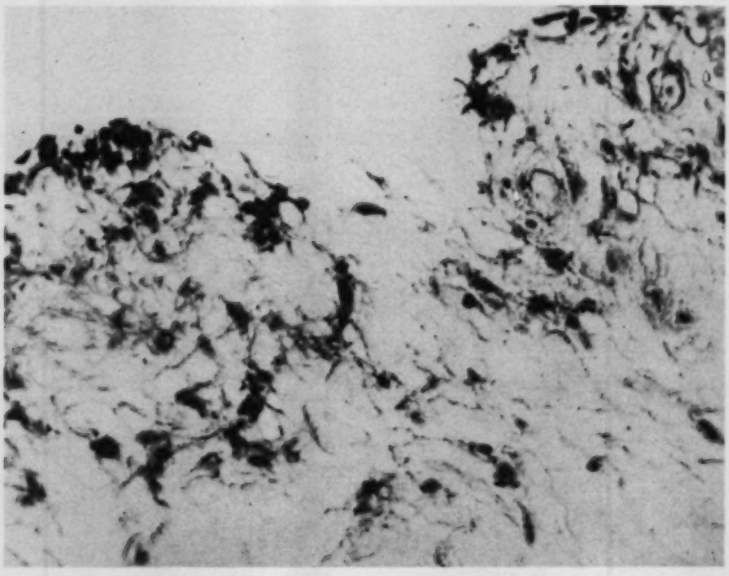


Fig. 11 (François, Neetens and Collette). The area shown by arrow (a) in Figure 10 is magnified to ×450. Fine argyrophilic fibers project from the iris stroma into the small crypt through areas where the anterior surface presents no continuous layer of cells or cell process. (Wilder reticulum stain.) An adjacent section at the same magnification is shown in Figure 12. (Courtesy of Dr. Zimmerman.)

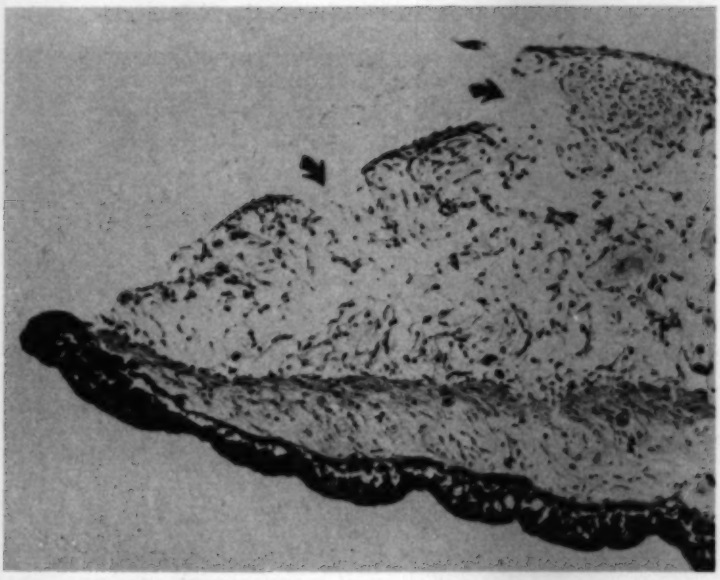


Fig. 12 (François, Neetens and Collette). Section adjacent to area (a) in Figures 10 and 11 but stained with hematoxylin-eosin is illustrated at the same magnification for comparison. Observe the absence of a continuous layer of cells on the anterior iris surface in the areas indicated by arrows. (Hematoxylin-eosin, ×112, courtesy of Dr. Zimmerman.)

Fig. 13 (François, Neetens and Collette). This section is adjacent to the one shown in Figure 11 but is stained with hematoxylin-eosin. The absence of the continuous cellular membrane on the anterior iris surface is illustrated especially well at the sites indicated by arrows. (Hematoxylin-eosin, ×450, courtesy of Dr. Zimmerman.

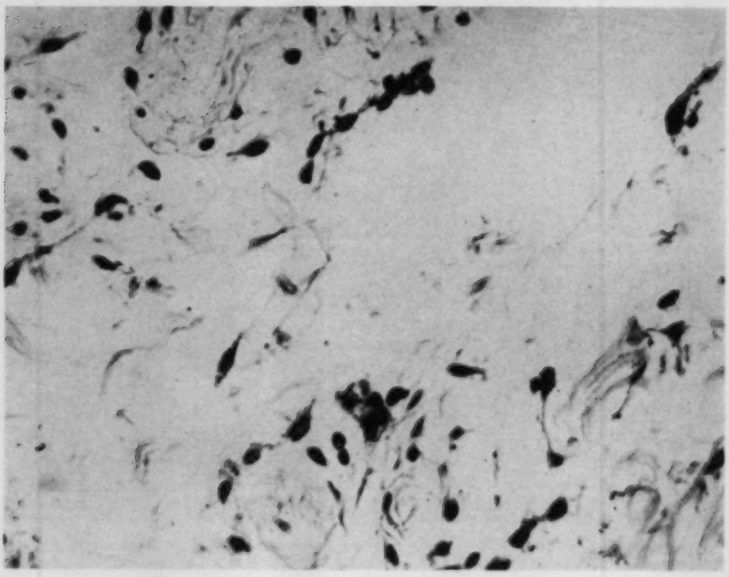
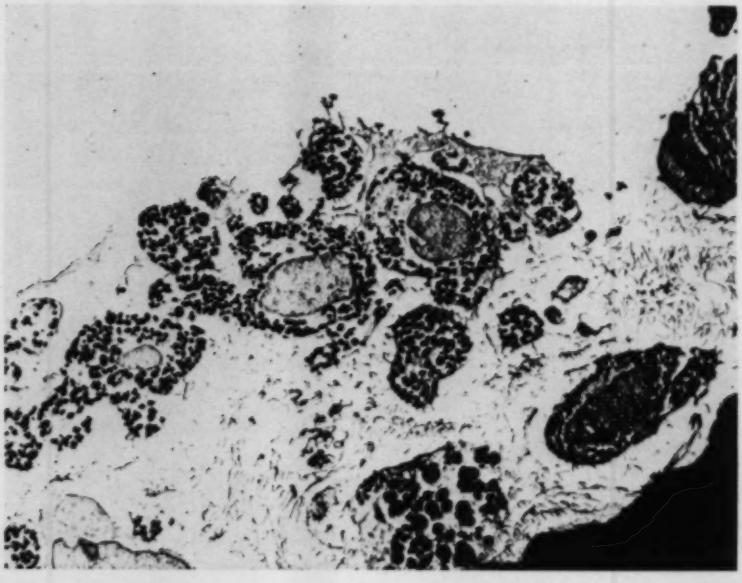


Fig. 14 (François, Neetens and Collette). Several large areas seemingly devoid of an anterior border layer of cells may be observed along the edges of the crypt present in the upper right-hand corner. (Hematoxylin-eosin, ×450, courtesy of Dr. Zimmerman.)



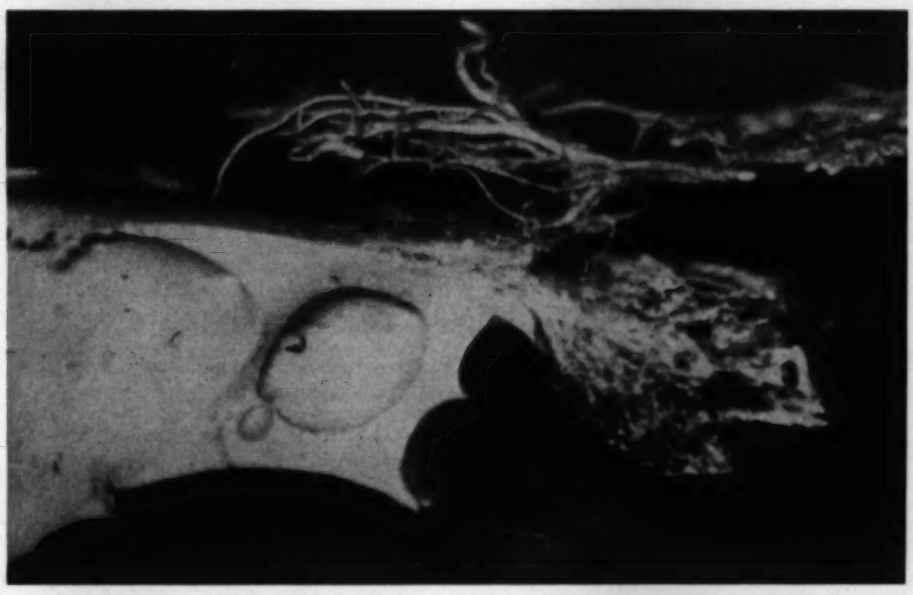


Fig. 16 (François, Neetens and Collette). Injection of Tygon into the anterior chamber of the cat under high pressure, with digestion by NaOH. Image of ciliary processes (below). (×120.) (Courtesy of F. Macri, National Institute of Neurological Diseases and Blindness, Bethesda, Maryland, Director, L. von Sallmann, M.D.)

superficial layer but anywhere in the mesodermal layer.

The visualization of the ciliary body and scleral vessels by injection of Tygon in the anterior chamber of the cat by Macri cannot be considered, the scleral tissues at the level of the anterior outflow paths not having been removed (fig. 16).

The nature, significance and origin of the canalicular network described have not hitherto been satisfactorily explained.

For the time being, it must be sufficient to observe its existence. Without other additional evidence, it cannot be admitted that a different outlet for aqueous humor is involved here.

The hypothesis can be put forward, however, that this network is connected with the venous plexus of the ciliary body, the pars plana and the choroid.

Summary

Microradiographic examination of the human iris following perfusion of the anterior

←

Fig. 15 (François, Neetens and Collette). Electron micrograph of a radial section of human iris anterior surface. The tissue was treated with buffered osmium tetraoxide within half an hour after enucleation, subsequently dehydrated and embedded in methacrylate. Section thickness was approximately 0.1 micron; the methacrylate was removed with Xylene; shadow cast at arc tan ⅓ with uranium and then examined in the electron microscope. On this electron micrograph, the cells along the anterior surface do not appear to form an uninterrupted membrane. Both in monkey and man, numerous openings are seen in sections between the cells on the surface. Filaments between cells show 640 Å periodicity, typical banding of "mature" collagen. The dense particles in the cytoplasm of the cells are the pigment granules. (Courtesy of Ben S. Fine, M. D., and A. J. Tousimis, Sections on Biophysics and Ophthalmic pathology, Armed Forces Institute of Pathology, Walter Reed Medical Center, Washington 25, D.C.)

chamber under physiologic pressure with Thorotrast has revealed a canalicular network which differs from the vascular network and is characterized by radial ducts in the central part and circular ones in the peripheral part of the iris.

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ACTINOMYCOTIC LACRIMAL CANALICULITIS*

A report of two cases with a review of the characteristics which identify the causal organism, Actinomyces israelii

Leo Pine, Ph.D., Hilliard Hardin, Ph.D., and Larry Turner, M.D.
Durham, North Carolina
and
Shaler S. Roberts, M.D.
Florence, Alabama

Infections of the eye, due to organisms belonging to the actinomycetes, have been described in the literature under a variety of clinical terms such as streptothricosis, leptothricosis, nocardiosis and actinomycosis. The clinical usage of these terms would imply, therefore, that the etiologic agents responsible for such infections belonged, respectively, to the genera Streptothrix, Leptothrix, Nocardia and Actinomyces. However, one finds that Streptothrix or Leptothrix has been used when, indeed, the infection was caused by Actinomyces.[2,3,7] Moreover, the names Streptothrix or Leptothrix has been applied to the aerobic actinomycete, Nocardia, as well as to the anaerobic actinomycete, Actinomyces.[4-6] Also, the use of a binominal composed of two generic names, Streptothrix actinomyces,[6] further complicates the etiologic nomenclature of eye infections caused by this group of organisms.

Since Nocardia[4,13,14] and Actinomyces[8-12] not only cause localized infection of the eye but also cause systemic infection and, furthermore, since these organisms respond differently to therapeutic agents,[15-17] it would seem desirable to attempt a definitive bacteriologic identification of an eye infection caused by members of the actinomycetes. In view of these considerations the history of two patients with lacrimal canaliculitis, caused by Actinomyces israelii, will be discussed and the history and definitive characteristics of actinomycetes which cause eye infections will be reviewed.

Case reports

Case 1

R. R., a six-year old white boy, was referred to the Eye Clinic, McPherson Hospital, on September 28, 1958 with the chief complaint of intermittent discharge from the right eye which had not responded to treatment with "a number of different kinds of eyedrops" during the past three years. His history was of interest in that he had been hospitalized three years previously with a severe acute conjunctivitis of the right eye which coincided with a "good take" of a smallpox vaccination of an older sister.

Eye examination revealed 20/20 vision in each

* From the Microbiology Department and Department of Ophthalmology, Duke University School of Medicine, and the Eye Clinic, McPherson Hospital, Durham. The research reported in this article was supported, in part, by Grant E1866 from the National Institute of Allergy and Infectious Diseases, United States Public Health Service, Bethesda, Maryland.

eye. There was moderate induration of the right lower eyelid near the inner canthus about the area of the punctum and the canaliculus. There was also moderate injection of the bulbar and palpebral conjunctiva in this area. The remainder of the eye examination revealed no further abnormalities.

On October 20, 1958, the patient returned to the hospital for examination of the right lower canaliculus and lacrimal duct under general anesthesia. The right lower punctum was dilated and a large number of hard, yellow concretions were removed by expression and with the use of a small chalazion curette. When the canaliculus was free of concretions, it was found to be obstructed. Attempts to probe and irrigate with normal saline were unsuccessful. The upper punctum was dilated and the canaliculus was irrigated with saline passing freely into the nose. The material removed from the lower canaliculus was taken to the laboratory for smears and culture.

Impression: (1) Stenosis, right lower canaliculus; (2) actinomycete infection, right lower canaliculus.

The patient was discharged from the hospital on the following day with instructions to use Chloromycetin eyedrops; one drop to be instilled in the right eye every two hours while awake. When seen on October 6, 1958, two weeks later, the conjunctivitis had subsided and there was no discharge from the eye.

Case 2

R. L. H., a 14-year old white boy, was seen in the Department of Ophthalmology, Duke University Medical Center on July 28, 1958, with the chief complaint of a creamy discharge at the corner of his left eye which had been noted particularly in the morning for the past year. On a previous visit, six months earlier, he was found to have acute conjunctivitis of the left eye and a minimal amount of simple myopia. At this time he was placed on Gantrisin drops and corrective lenses were prescribed. The conjunctivitis subsided but a continuous discharge from the eye necessitated a return to the clinic.

On the present visit the ophthalmologic findings, except for minimal amount of simple myopia, were confined to the left eye. The palpebral conjunctiva was somewhat hypertrophied and had a red velvet appearance. The cornea was not involved. The median portion of the left upper lid was swollen, having the appearance of a small chalazion adjacent to the inner canthus. The superior and inferior puncta were dilated and lacrimal probes were passed easily into the lacrimal sac; there was no obstruction to irrigation.

The median portion of the left upper lid was anesthetized, sharp scissors were introduced into the superior punctum and a small medial incision was made. The superior canaliculus was explored with a small chalazion curette. A cystic enlargement of the canaliculus approximately two mm. superiorly and extending nasally for approximately three to four mm. was found. Many small, discrete, yellowish-white bodies were removed from the cavity with the curette. Neosporin ointment was instilled and a dressing placed over the left eye. The material removed from the canaliculus was taken to the laboratory for smear and culture.

Impression: actinomycete infection, left superior canaliculus.

The patient was seen two days later at which time there remained a moderate amount of swelling and inflammation just above the superior punctum, and pressure over this area expressed a small particle similar to those removed previously. At this time the patient was given a suspension of achromycin ophthalmic oil and instructed to instill drops into the left eye four times daily and to return in one week for further evaluation.

On his return to the clinic on August 6, 1958, it was noted that the swelling was greatly reduced. However, a small amount of pus could be expressed. The area was again anesthetized and a large yellowish mass was removed from the dilated canaliculus with a small chalazion curette. Achromycin drops were continued and, when the patient was next seen on August 12th, there was no indication of recurrence and irrigation through the superior punctum was performed with no difficulty. Medication was continued for approximately one more month and the patient has had no further difficulty.

Bacteriologic studies

Material removed from the lower canaliculus of patient R. R. was inoculated into tubes of thioglycollate broth. After several days growth at 37°C., gram-stained smears from these cultures showed both typical actinomycotic elements and staphylococci. The mixed culture was streaked on plates of glucose casitone medium[18, 19] which were incubated at 37°C. under anaerobic conditions. Single spidery colonies typical of Actinomyces israelii were picked to tubes of stock medium to establish pure cultures for study. The culture was labeled OS 131.

Material, in the form of yellowish-white concretions, removed from the left superior canaliculus of patient R. L. H. was washed with sterile distilled water, crushed and inoculated into stabs of glucose casitone medium which were incubated at 37°C. under anaerobic conditions. Inoculum from the resulting growth was streaked on glucose casitone agar plates, as above, and single colonies typical of Actinomyces israelii were picked to establish pure cultures. The culture was labeled #699. A complete bacteriologic description of Actinomyces israelii, strains OS 131 and #699, has been pre-

sented elsewhere.[1] However, in the following discussion, the pertinent characteristics of these strains will be related to the characteristics of the species as a whole.

A. israelii is an anaerobic, gram-positive, nonacid-fast, branching micro-organism which is an obligate parasite of man and animals. It is not found free in nature and has not been cultured from soil. In this respect, it differs markedly from the other members of the actinomycetes, Nocardia and Streptomyces, which are saprophytic, aerobic, soil-inhabiting organisms.[32, 41, 43, 56] A. israelii is found in the mouth, generally associated with salivary calculus.

This anaerobic or microaerophilic organism readily fragments to form bacillary or diphtheroid elements (fig. 1). On agar medium it forms small spreading "spider" colonies which gradually increase in size to approximately two mm., becoming white and opaque with a raised convex surface (fig. 2). In general, those colonies formed by strains isolated from a typical case of human actinomycosis become rough and granular in appearance. This type of colony is referred to as a "molar tooth" form (fig. 3). The colonies also may be completely circular and convex with a smooth shiny surface. However, a rough colony may become smooth as a result of the medium used or as a result of continued transfer.

Smith[12] observed that only two strains of 11 of Actinomyces which he had isolated from the eye formed rough colonies at first; however, on subsequent transfers, the colonies became smooth. The remaining strains were smooth on isolation. Strains OS 131 and 699 also formed smooth colonies (fig. 3). It would, therefore, appear that this is a characteristic which is particularly associated with those strains isolated from the eye.[1, 8, 12]

When transferred to a liquid medium, such as fluid thioglycollate, A. israelii may grow slowly forming compact granules which readily settle to the bottom of the tube leaving the supernatant clear. Or, more rarely, it may grow rapidly forming a few initial granules which develop streamers of diphtheroid cells causing the medium to become turbid. As already mentioned, the type of growth is often influenced by the composition of the medium. The variations of growth exhibited in solid and liquid media by different strains of A. israelii have been

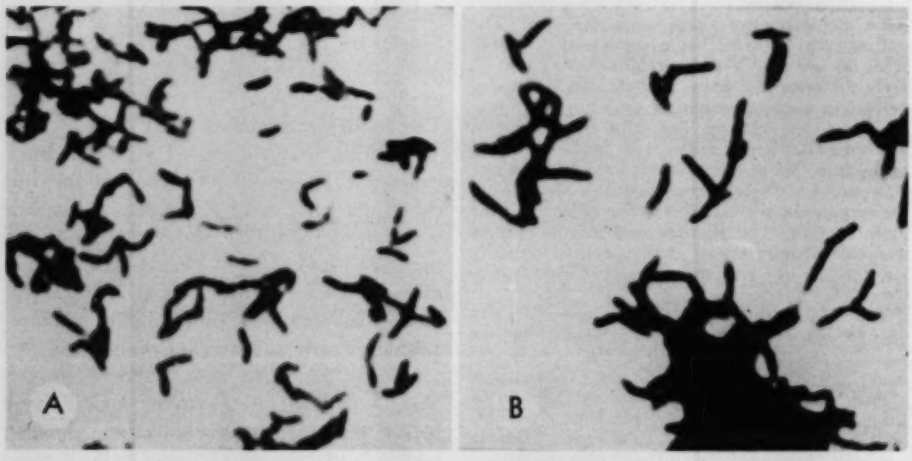

Fig. 1 (Pine, Hardin, Roberts and Turner). Microscopic appearance of strains of Actinomyces israelii isolated from the lacrimal canal and human actinomycosis (Gram stained, ×2200). (A) Strain OS 131, isolated from the lacrimal canal. (B) Strain 895, isolated from a typical case of thoracic actinomycosis.

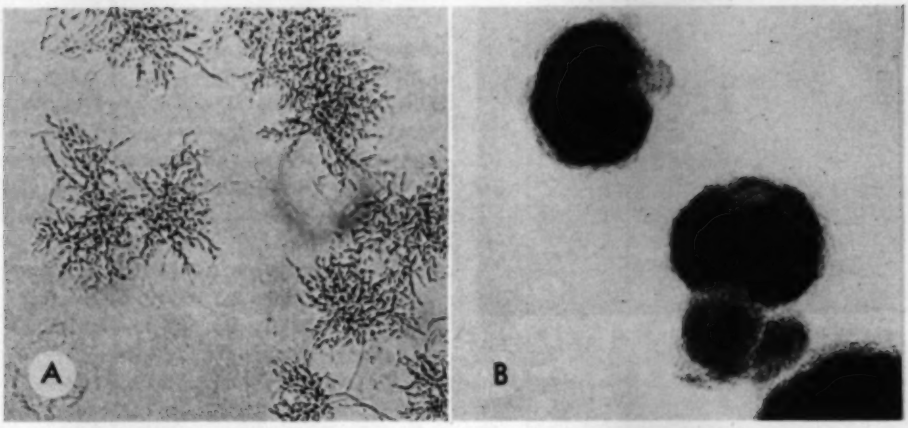

Fig. 2 (Pine, Hardin, Roberts and Turner). Microscopic appearance of Actinomyces israelli, strain OS 131, isolated from lacrimal canaliculitis. (A) Two-day old "spider" colonies (transmitted light, ×360). (B) Five-day old colonies (transmitted light, ×128).

reviewed by Rosebury.[33] In respect to strains #699 and OS 131, the former grew rapidly causing the medium to become turbid; whereas, the latter grew slowly developing granules and the medium remained clear (fig. 4).

It is difficult to cause disseminated infections in animals, but local abscesses are easily formed by intradermal inoculation.[37-39] Although these abscesses generally rupture and heal within seven to 10 days, true mycelial elements are generally formed in this time and may be readily observed in smears stained by the gram stain (fig. 5).[40]

Physiologically, A. israelii is characterized as a strict anaerobe or as a microaerophile,

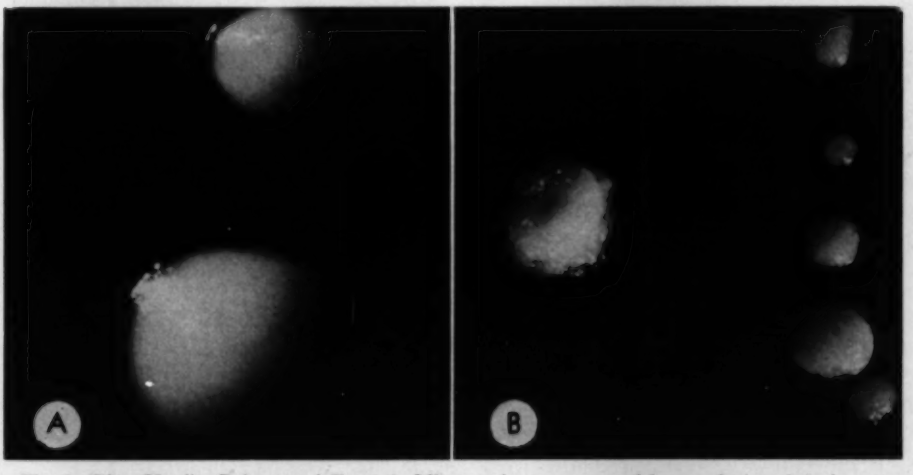

Fig. 3 (Pine, Hardin, Roberts and Turner). Microscopic appearance of large colonies of Actinomyces israelii. (A) Strain OS 131 isolated from lacrimal canaliculitis (reflected light, ×28). (B) Strain 895 isolated from a typical case of thoracic actinomycosis in man (reflected light, ×13). Note the typical "molar tooth" colony formed by this strain.

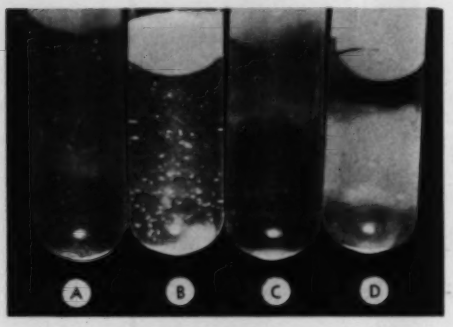

Fig. 4 (Pine, Hardin, Roberts and Turner). Growth of Actinomyces israelii in broth with 0.05-percent agar. (A) Strain OS 131, isolated from lacrimal canaliculitis, grown in brain heart infusion broth. (B) Strain OS 131 grown in glucose-casitone broth. (C) Strain 699, isolated from lacrimal canaliculitis, grown in brain heart infusion broth. (D) Strain 699 grown in glucose-casitone broth.

although some strains are capable of growing facultatively under certain conditions.[33,34] This growth characteristic and those mentioned above, smooth colonies on agar and turbid growth in liquid media, as well as microscopic morphology, have made difficult the differentiation of Actinomyces from anaerobic diptheroids. However, members of the genus Corynebacterium are catalase positive and this test serves as a simple and rapid means for distinguishing these two types of organisms.[35,36]

A. israelii is catalase negative, does not liquefy gelatine, digest casein or cause true hemolysis of blood.[35] Litmus milk is generally reduced and a soft curd may be produced. Formation of H_2S or indole, hydrolysis of starch or reduction of nitrate may vary with the strain. Sugars such as glucose, maltose, lactose and sucrose are fermented with the formation of acid but no gas, while mannose and xylose may support only poor growth with little or no acid formation.[24,26,33] Acetic, formic, lactic and succinic acids are formed as a result of glucose fermentation.[34] Strains OS 131 and #699 formed acetic, formic and lactic acids; succinic acid was not determined. In addition, it was found that strain 699 also formed propionic acid.[1]

Strains of Actinomyces are sensitive to penicillin, aureomycin and Chloromycetin; they are much less sensitive to sulfa drugs. They do not develop resistance to antibiotics or drugs in vitro[57] although some small degree of resistance may develop in the patient during treatment.[15,58] Penicillin is considered to be the drug of choice for the treatment of infections caused by Actinomyces israelii, particularly for systemic infections when the patient must be treated for a period of weeks or months. Sulfa drugs have been of little value in systemic or localized actinomycosis. Topical application of a variety of antibiotics in localized infections, such as actinomycotic canaliculitis, has proven beneficial. One must run the risk,

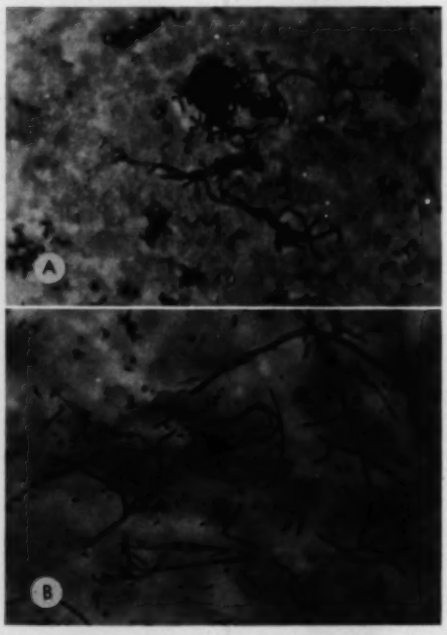

Fig. 5 (Pine, Hardin, Roberts and Turner). Mycelial elements of Actinomyces israelii in the pus from inoculated hamsters (Gram stain, ×1100). (A) Strain OS 131, isolated from lacrimal canaliculitis. (B) Strain 699, isolated from lacrimal canaliculitis.

however, of creating sensitivity to a particular antibiotic by its use in topical medication.

As already mentioned, Nocardia asteroides is a saprophytic, strictly aerobic fungus which may be isolated from the soil. It forms light yellow to orange adherent colonies which may be smooth or rough in outline with a fuzzy to smooth surface. As the mycelium fragments into bacillary and coccoidal forms, the surface of the colonies may become powdery in appearance. Microscopically, the mycelium grows as slender, radiating branching filaments over the agar surface. The cells are gram positive and are usually acid fast if a modified acid-fast staining procedure is used.[42] This characteristic is often rapidly lost when the fungus is grown on general laboratory media, but it is often regained when the fungus is grown in litmus milk. Although the genus Nocardia is described as not forming chains of aerial spores,[26] such spore formation has been observed in some strains.[41]

The individual physiologic characteristics of N. asteroides are not by themselves definitive. In general, strains of N. asteroides will be negative on most of the following reactions: hydrolysis of casein, decomposition of tryosine, and acid production from lactose, maltose, xylose, mannose, mannitol and inositol.[43, 56] In litmus milk, N. asteroides may form an orange-colored ring or pellicle but the milk is not coagulated nor peptonized. It will utilize paraffin for growth. It is considered to be the most pathogenic of the disease-producing Nocardia species, and when it is inoculated in high concentrations into guinea pigs they usually die in seven to 10 days.[32]

When stained in tissue sections, N. asteroides is generally acid-fast while A. israelii is never acid-fast. In disseminated nocardiosis, abscesses are formed in which N. asteroides does not form sulfur granules nor elicit a granulomatous tissue reaction. On the other hand, in cases of actinomycosis, A. israelii generally, but not always, forms sulfur granules and the tissue reaction is granulomatous. However, in cases of chronic, limited nocardiosis (mycetoma), N. asteroides does form true sulfur granules with a granulomatous tissue reaction. Therefore, dependent upon the clinical material, the mycelial elements of the two organisms in stained preparations may appear identical. In the absence of a definitive acid-fast stain or sulfur granules, pure cultures must be isolated to identify the causal organism.

History and nomenclature

Although clinical cases of fungal infections of the lacrimal canal were first observed by von Graefe[52, 53] in 1854 and 1855, no adequate description of the fungus was made until 1875. At this time Cohn[20] described, but did not culture, a fine branching fungus which he observed in lacrimal concretions given to him by Prof. Foerster. Because he considered the fungus quite different from the nonbranching organism Leptothrix buccalis, he named the fungus Streptothrix foersteri. Bollinger,[27] in 1877, gave the first clinical description of actinomycosis in cattle and the causal organism observed in these tissues was described and named Actinomyces bovis by Harz.[21] Shortly thereafter, Israel[28] described a case of actinomycosis in man and Ponfick[29] compared and related the characteristics of the human and bovine diseases.

Bostroem,[51] in 1890, was the first to culture successfully an aerobic actinomycete. Although the material used to inoculate the tubes was clinical material obtained from actinomycosis in cattle, in all probability these cultures were contaminants.

A year later, however, Wolff and Israel[22] successfully cultured the anaerobic actinomycete from cases of human actinomycosis. Their classical description of the morphology and physiology of this anaerobic fungus thus enabled subsequent workers to identify, with certainty, and establish the organism as a cause of actinomycosis in man.[37]

In 1900, Silberschmidt[54] was the first to culture successfully the anaerobic actinomycete from lacrimal concrements. A year later he isolated a strain from maxillary actinomycosis of a cow and compared it with strains isolated from the lacrimal infections and from cases of maxillary and thoracic actinomycosis in man.[55] All the strains were considered to be identical. Silberschmidt[54] had also considered the validity of the names Actinomyces and Streptothrix and concluded that the name Streptothrix was the correct one to be used.

As a result of the successes in isolation, there was a very great increase in the numbers of publications describing the morphology and cultural characteristics of strains of actinomycetes isolated from man and animals. However, a critical review of the literature suggests that many of the cultures were contaminated. This, with variations in observations of different workers and the differences in opinion regarding the correct nomenclature of the organisms, lead to the taxonomic confusion which followed. Finally Breed and Conn,[23] approximately 20 years later, reviewed the literature pertaining to taxonomy and concluded that the name Actinomyces was the name most valid according to the rules of nomenclature and usage.

As a result of this study, the name Actinomyces bovis was applied to the anaerobic actinomycete causing human and bovine actinomycosis. Erikson,[24] however, compared strains of Actinomyces isolated from both human and bovine sources and on the basis of colony morphology, growth characteristics, and serology, she concluded that the bovine strains were sufficiently different from the human form to warrant species separation. Consequently, she restricted the name Actinomyces israelii to those strains which, isolated from man, grew slowly to form small, granular or rough colonies in liquid and on solid media; whereas, the name A. bovis was used for those strains which, isolated from a cow, grew rapidly and formed smooth, circular, soft colonies on solid media or formed turbid growth in liquid media.

Although many workers do not at present accept this division of species, her conclusions were supported by the work of Thompson[25] and both species are described in the latest edition of Bergey's manual of *Determinative Bacteriology*.[26] The name Streptothrix used in the late nineteenth century as a synonym for both anaerobic and aerobic actinomycetes, is restricted to members of a higher order of true fungi and is no longer applicable to the actinomycetes. The name Leptothrix, which is often used in the ophthalmologic literature, is now a generic name applied to a gram-negative, nonbranching ensheathed bacterium commonly found in ponds. It is nonpathogenic and totally unrelated to the genus Actinomyces.

It is unfortunate, but apparent, that at some time during the early twentieth century the bacteriologists and ophthalmologists lost sight of their mutual interests in lacrimal actinomycosis. For example, in their consideration of the validiy of the species name, Breed and Conn[23] stated "reference to Cohn's original description of S. foersteri shows that the only possible way in which this species can be recognized is in case it is shown that its habitat (concretions in the human tear duct) was sufficiently characteristic to identify it."

That this was the case had already been shown by numerous ophthalmologic publications which established the fact that the fungus in the lacrimal canal was an anaerobic actinomycete.[30, 31, 54, 55] On the other hand, even though the fungus had been periodically described as Actinomyces, many ophthalmologic papers continued to reflect the confusion in nomenclature which remained. Many investigators no longer associated the Streptothrix or Leptothrix with the Actinomyces which caused systemic actinomycosis. Likewise, some did not differentiate between the aerobic and anaerobic actinomycetes which caused eye disease.

Review of actinomyces infections of the eye

According to Birge,[2,7] obstructions of the nasolacrimal duct with mycotic plugs may be seen as often as once or twice a year. Duke-Elder[6] states that a conjunctival infection with Streptothrix is rare. When it does occur, it is usually found in concretions in the lacrimal canaliculus. Our experience has shown that this condition is by no means rare but it is certainly uncommon. According to Duke-Elder, when the conjunctivas are involved, small yellow nodular lesions may be present which represent accumulations of the organisms. There may be an obstinate catarrhal conjunctivitis of the angular type or even a membranous conjunctivitis. An acute infection with formation of yellow follicles on the conjunctiva and pharynx with preauricular adenopathy has been described. This description of actinomycotic infection, given in Duke-Elder, may be expanded and certain points emphasized.

Concretions, due to Actinomyces, may occur in the superior or in the inferior canaliculus as indicated in the two case reports here. If the inferior canaliculus is involved, the first symptom is usually epiphora.

Elliot[44] points out that two clinical types of the disease may be recognized: (a) those with the canalicular signs predominating and (b) those with marked conjunctival reactions but with no apparent canalicular signs. The latter condition is unilateral and the conjunctiva adjacent to the punctum may be mildly inflamed. There may also be an acute conjunctivitis of both the palpebral and the bulbar conjunctivas. There may be considerable mucosecretion on the lid margin and the suppuration may be greater than suggested by the appearance of the conjunctivitis. Acute catarrhal corneal ulceration may also occur.

Smith[12] emphasized that the symptoms of conjunctivitis may be observed before the infection of the lacrimal canal is recognized. In one of his patients the infection was of four and a half years' duration before concretions were observed in the lacrimal canal. In the case R. R., described in this report, three had a half years passed before the discovery of lacrimal concrements. Smith also pointed out that the concretion is usually attached to the wall at one point; thus it may block the flow of tears without preventing syringing of the lacrimal canal.

Invariably cures are effected simply by removal of the concrements from the lacrimal canal. However, it is difficult to effect a cure of acute conjunctivitis without the use of antibiotics.[44]

The extent of tissue damage or invasion by A. israelii may vary. In one case reported here (R. R.) the possibility exists that the blockage found in the right lower punctum was a result of the infection. Moore[10] reports one case in which the fungus had eroded through the wall of the canaliculus onto the conjunctival surface. In the case reported by Ridley and Smith[45] the preauricular lymphatic gland was enlarged in a membranous infection of the lower eyelid. When the conjunctivitis was treated with aureomycin, the preauricular gland became fluctuant and upon aspiration and culture of the purulent material the organism was isolated. Similarly, Wright[46] observed an enlargement of the perauricular, parotid and submaxillary glands. In these later cases, the bacteriologic description strongly suggested that the causal organism was Actinomyces. Unfortunately, in the case of acute streptothrix infection reported by Knapp and Dwyer,[47] it would be difficult to decide whether the organism isolated was Actinomyces or Nocardia.

Although both of the patients reported here were male, it has long been recognized that Actinomyces infections of the lacrimal canal most frequently occur in women.[48] This is emphasized in the report by Elliot[44] of nine cases, all in females, ranging from nine to 58 years of age. Moore[10] reported six cases, all in females. In the 15 cases observed by Smith[12] three were in males, the rest were of females ranging from 40 to 58 years in age.

Recognizing that Actinomyces is a parasite living in the mouth, one might explain this predominance of infections in women. They are more apt to stifle an explosive sneeze, the force of which might project the organism into the lacrimal canal. Perhaps the greater tendency to cry with blowing of the nose serves to carry the organism directly into the lacrimal canal, or wiping of the eyes serves to carry the organism indirectly from the mouth to the eye via the hands. A third mechanism of infection might be the often observed habit of removing material from the corners of the eye with a finger well moistened with saliva.

Whatever the mechanism of infection, one is struck by the fact that of all the cases reported there has been no case in which a primary infection of the eye progressed to acute disseminated actinomycosis. Probably the site of the infection is such that the fungus is limited to the lacrimal canal and cannot invade the tissues unless they have been sufficiently traumatized. This is undoubtedly what occurs in actinomycosis following tooth extractions which result in "lumpy jaw" in man. One case of acute conjunctivitis reported by Elliot,[44] was actively treated for one year and a second required two years of prolonged treatment; yet, systemic invasion did not occur.

In our review of the cases of actinomycotic infections of the eye, those which were unquestionably due to Nocardia were limited. The fungus has been definitely isolated from a corneal ulcer by Schardt, Unsworth, and Hayes.[14] Bruce and Locatcher-Khorazo[4] described an aerobic actinomycete isolated from conjunctival scrapings in a case of punctate keratitis, which from its description may have been a nocardial species.

Benedict and Iverson[13] reported a case of chronic keratoconjunctivitis from which a strain of Nocardia was isolated eight times during a four-year period of treatment. The Nocardia was described as being acid-fast and forming light yellow colonies. It was most probably N. asteroides.

Recognition that both genera of fungi may cause conjunctival infections emphasizes the fact that simple microscopic observation of stained clinical material does not suffice to identify the causal organism. Although we are not aware of any report of a case of lacrimal infection by Nocardia, other genera of fungi have been found in the lacrimal canal.[49] In view of the increased number of fungal infections of the eye, due to the use of steroid therapy,[50] the possibility of acute nocardial infection of the lacrimal canal and conjunctiva remains a strong possibility.

Summary

Two cases of actinomycotic canaliculitis have been presented. An attempt has been made to clarify some of the confusion in the ophthalmologic literature concerning the nomenclature of actinomycotic diseases of the eye. The bacterial identification and treatment of these causative fungi are given. The literature on actinomycotic infections of the eye has been reviewed.

Duke University Medical School.

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THE USE OF AMPHOTERICIN B IN SELECTED CASES OF CHORIORETINITIS*

HAROLD F. FALLS, M.D., AND CONRAD L. GILES, M.D.
Ann Arbor, Michigan

Coincident with the advent of antibiotics and steroids the ophthalmologist has been confronted with an increased incidence of ocular fungus disease. Any therapeutic agent which exhibits fungicidal properties, therefore, warrants careful appraisal by our discipline. This is particularly significant in that most fungus diseases of the eye have been relatively resistant to current antifungal therapy.

Amphotericin B, an antibiotic derived from soil Streptomyces, exhibits a most promising antifungal spectrum. Of pertinent interest to this investigation is the specificity that this agent shows toward the organism Histoplasma capsulatum. The available evidence implicating Histoplasma capsulatum as an ocular pathologic agent is admittedly tenuous. The particular characteristic, however, of this organism to exhibit widespread involvement of the reticulo-endothelial system and its unique mimicry of tuberculosis makes it appear quite likely that it may be pathologic to ocular tissues. Histoplasmosis has previously been implicated as a probable case of human iridocyclitis and chorioretinitis. It is the purpose of this presentation to summarize a limited and prelimi-

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nary experience with amphotericin B* as a therapeutic agent in the management of suspected histoplasmosis chorioretinitis.

Amphotericin B

A. History

Gold[1] and his co-workers isolated the amphotericin A and B from Venezuelan soil in 1955. It soon became apparent that these agents possessed no antibacterial action. Laboratory and clinical evidence quickly accumulated, however, indicating that these antibiotics possessed important fungicidal properties. Amphotericin A presented a much wider antifungal spectrum than B, but the latter exhibited greater potency against the common deep fungal pathogens including: Histoplasma capsulatum, Coccidioides immitis, Candida albicans, and Cryptococcus neoformans.[1]

Oral administration of amphotericin B proved fairly efficacious in the management of the deep mycoses but, because of erratic gastrointestinal absorption, therapeutically desirable blood serum or cerebrospinal fluid levels were not consistently obtained.[2] A water-insoluble intravenous preparation became available in 1956 and early in 1957 a water-soluble amphotericin B mixture was developed.[3] The employment of these two forms resulted in exciting clinical and experimental developments.

B. Administration

At present most clinicians administer amphotericin B by intravenous infusion. The exact dosage, amount of diluent and timing of administration have not been completely ascertained. Most clinicians recommend dosages between 0.50 and 1.5 mg./kg. of body weight given daily and diluted in at least 10 cc. of five-percent glucose per mg. of amphotericin B.[2,4,6] Drs. Harrell and Curtis[7] of The University of Michigan Medical School, Department of Dermatology, have successfully evolved the following regimen: Daily intravenous infusion of 50 mg. of the drug in 500 cc. of five-percent glucose for 10 to 25 days. Adequate serum and cerebrospinal fluid levels can be maintained for 24 to 36 hours in this manner.[2,6]

Vogel[6] was able to inhibit therapeutically Histoplasma capsulatum in two of his cases by administering the drug on alternate days. Many of the toxic side-effects of the drug, moreover, can be minimized when it is so administered. Curtis[8] and more recently Christie[9] have recommended the employment of the sulfonamides in the treatment of histoplasmosis. Christie has presented evidence revealing that triple sulfonamides, used alone, have been successful in the treatment of a number of cases of systemic disease. It is not known if these two agents, sulfadiazine and amphotericin B used in combination, would be more efficient therapeutically, although experimental evidence suggests that this may be the case.[10]

C. Side-effects

Seabury,[11] in a careful analysis of the side-effects of amphotericin B therapy in 18 cases, tabulated in the order of their frequency the following: chills and fever (17), anorexia (10), abdominal pain (8), headaches (7), nitrogen retention (6), nausea (4), vomiting (1), melena (1), phlebitis (1), and hemorrhagic gastro-enteritis (1). One case of exfoliative dermatitis, purpura and death was reported by this author.

The kidney appears to be the organ most vulnerable to amphotericin B toxicity. This is manifested by an azotemia. Prolonged therapy produces a rising blood urea nitrogen which fortunately is reversible upon cessation of therapy. Once the blood urea nitrogen has returned to normal it is believed safe to resume administration.

Squibb Institute for Medical Research workers have reported that amphotericin B can produce diffuse gastro-intestinal hemorrhages in dogs. Seabury[11] found gastro-in-

* We wish to thank the Squibb Institute for Medical Research for making available the supply of amphotericin B (Fungizone, Squibb) utilized in this study.

testinal bleeding in a male treated with amphotericin B for blastomycosis. Autopsy of the individual revealed lesions similar to those that occurred experimentally in the dog. It was believed, however, that death was due to blastomycosis in this patient. The same author encountered melena in another patient.

Various measures to counteract many of these side-effects have been employed. Seabury used large doses of salicylates in combination or alone with phenergen, benadryl, and concomitant steroid administration, while Lerner[12] reduced chills and fever with one gm. of aspirin given with the infusion and repeated every three hours as necessary.

It is apparent that amphotericin B therapy is not without danger and, in fact, could possibly cause death. The decision to use amphotericin B in the treatment of ocular histoplasmosis is not to be lightly made and if undertaken warrants extremely cautious and alert observation.

Histoplasmosis

Human infestation with Histoplasma capsulatum is startingly prevalent! It has been estimated that over one fifth of this country's population is infected and recently an authority suggested that as many as 500,000 cases occur yearly.[13]

Darling[14] reported the first case but failed to recognize that the etiologic agent was a fungus. DeMonbreun[15] laboriously and ingenuously demonstrated the fungus nature of the causative agent.

Histoplasmosis was long considered a uniformly fatal disease until Amos Christie[16] recognized the relationship of histoplasmosis sensitivity and pulmonary calcification in nonreactors to tuberculin. It soon followed that a benign, nonprogressive form of the disease existed and was undoubtedly far more common than the fatal progressive type.

A. Pathology

The causative organism, Histoplasma capsulatum, is parasitic (yeast phase) to the reticulo-endothelial system of the body and exists as a mold form (mycelial phase) at room temperatures. The pathologic response is a granuloma accompanied by giant cell formation, mimicking the tubercle of tuberculosis. Generalized miliary dissemination may occur, but usually the pulmonary system only is involved. Apical pulmonary cavitation may result from progression, or possibly from re-infections.

B. Epidemiology

The disease is world-wide in distribution but better than 50 percent of the cases have been reported from the Mississippi Valley area. Histoplasma capsulatum apparently is endemic, living in the soil and is transmitted to man, without any intermediate host, usually via the pulmonary route. Agricultural workers exposed to chicken dung, silos, storm cellars, and so forth are particularly vulnerable.

C. Clinical manifestations

It is beyond the scope of this paper to present a detailed analysis of the clinical variations of human histoplasmosis. The reader, therefore, is referred to Furculow's excellent summarization[13] of the five recognized categories: (1) mild histoplasmosis; (2) moderately severe histoplasmosis; (3) epidemic histoplasmosis; (4) acute disseminated histoplasmosis, and (5) chronic progressive histoplasmosis.

The disease may involve, aside from the pulmonary system, the gastro-intestinal tract, the genito-urinary system, the central nervous system (brain), middle ear, skin, skeletal system, joints and adrenals. The possibility of ocular involvement will be discussed later.

D. Diagnosis

A positive diagnosis of histoplasmosis, of course, requires demonstration of Histoplasma capsulatum through culture or microscopic study. Serologic tests, both pre-

cipitation and complement fixation, are valuable adjuncts to the diagnosis. A histoplasmin skin test and the blood studies are not positive until four to six weeks after the onset of active disease. These tests and agents are available through most state health departments.

A positive skin test can be looked upon as a valuable screening procedure and only indicates the presence of the disease in the individual at some time in life, while a complement fixation of greater than 1:8 is considered indicative of the presence of active disease.

Woods,[17] in his well-written textbook notes that to prove ocular histoplasmosis one would need to demonstrate the fungus directly in the intraocular tissues, fluids or exudates. Realizing the difficulty of obtaining such material, he outlined the provisions for making a tentative diagnosis of histoplasmosis as follows: (1) exclusion of other factors causing uveitis; (2) the presence of pulmonary calcification; (3) anergy to tuberculin, and (4) positive immunologic test for histoplasmosis.

E. Treatment

Until the discovery of amphotericin B the treatment of histoplasmosis was often inadequate. Sulfadiazine, stilbamidine and nystatin gave sporadic cures. It was not until the use of the intravenous preparation of amphotericin B that consistent therapeutic successes were reported. Friedman,[18] Miller, et al.,[19] and Greedyke and his group[20] each reported cases of systemic histoplasmosis resistant to previous regimens of treatment which responded dramatically to the employment of amphotericin B. Seabury[1] likewise found complete healing in patients who received intravenous therapy but no improvement in one patient treated with the oral preparation. Lehan's group[21] published results on five patients with systemic histoplasmosis who received intravenous amphotericin B, all of whom showed distinct improvement while receiving the drug.

Fig. 1 (Fall and Giles). Geographic distribution of histoplasmosis. (Modified after Furcolow.)

As the use of this agent has become more widespread, the documented cases of proven histoplasmosis treated with amphotericin B, have demonstrated the importance of this drug in our therapeutic armamentarium against the organism Histoplasma capsulatum.

Ocular histoplasmosis

As previously intimated, the evidence implicating Histoplasma capsulatum as a causative agent in the production of ocular disease is still presumptive. In this vein Woods[17] has written, "While Histoplasma capsulatum has not as yet been isolated from a human eye with granulomatous uveitis, thus fulfilling Koch's postulates, nevertheless the accumulated evidence points strongly to the probability that Histoplasma infection is an actual cause of granulomatous uveitis, and in this respect may ultimately prove to be the most important of the fungi."

Experimental evidence is available that Histoplasma capsulatum can produce uveitis in laboratory animals. Day[22] produced a granulomatous uveitis in rabbits by injecting Histoplasma capsulatum into their anterior chambers. He also reported data on four patients who exhibited positive histoplasmin skin tests, pulmonary calcification, and granulomatous uveitis. The patients failed to exhibit evidence implicating other causative agents.

A meticulous survey of the available liter-

ature reveals only three patients who have had culturally proven histoplasmosis and a concomitant uveitis. Reid[23] described a patient exhibiting: "small, white, irregular areas surrounded by hemorrhage in the ocular fundi . . . not unlike tubercles." Salvin and Furcolow[24] reported the presence of a "retinitis" in a patient, and a "nodular iritis" in another individual, both affected with proven histoplasmosis. In the latter two cases, however, a diagnosis of sarcoidosis was considered.

Krause[25] postulated the diagnosis of histoplasmosis uveitis in a patient who had exhibited the following findings: exacerbation of granulomatous uveitis following histoplasmin skin testing and disseminated discrete pulmonary calcification. The latter suggested either healed histoplasmosis or miliary tuberculosis. The tuberculin test was negative and, more important, a positive histoplasma complement fixation test was secured. Krause concluded that "the etiology of the patient's right macular chorioretinitis was evidently due to an infection with Histoplasma capsulatum."

A survey of the literature did not disclose that amphotericin A or B had been used to treat cases of presumptive ocular histoplasmosis. Foster and his associates,[26] however, treated a postoperative cataract extraction endophthalmitis in one human eye with intraocular, subcutaneous and subconjunctival amphotericin B. The eye was salvaged but was amaurotic. A volutella species of fungus was cultured from the involved eye.

Harrell and Curtis'[7,27] encouraging and successful management of systemic and dermatologic deep mycoses stimulated us to treat certain cases of granulomatous uveitis with this agent. Under the guidance and advice of these dermatologists patients were selected who exhibited the following findings: ophthalmoscopically suspicious chorioretinitis; a positive histoplasmin skin test; a negative or positive tuberculin skin test, and disseminated pulmonary calcification. Failure of the lesion to respond to other forms of therapy also strongly influenced selection of the patient, particularly antituberculous regimens in the cases having exhibited a positive tuberculin reaction. Complement fixation tests for histoplasmosis had to be secured through the State Health Department Laboratory. Since these reports were not infrequently long delayed, a positive histoplasmin complement fixation was therefore not required as an immediate requisite for eligibility for treatment with amphotericin B.

Case summaries

The pertinent facts concerning the nine cases of histoplasmosis chorioretinitis treated with intravenous amphotericin B are here summarized.

Case 1

Hospital number 853101. A man, aged 42 years, a resident of Michigan, presented ophthalmoscopic evidence of active central chorioretinitis, right eye, and inactive central chorioretinitis, left eye. The corrected visual acuity was 20/20 right eye and counting fingers left eye. The visual field exhibited a large paracentral scotoma in the right eye (2/1000 red) and a dense, moderate sized central scotoma in the left eye (2/1000 white).

Uveitis survey. The patient presented a positive histoplasmin skin test, a positive histoplasma complement fixation test (1:8), and pulmonary calcification compatible with histoplasmosis.

Therapy consisted of 0.5 gm. amphotericin B given intravenously in 10 divided doses over an interval of 10 days. Vasodilators and steroids (prednisilone) were also employed in addition to phenergen and aspirin.

Therapeutic side-effects. The patient exhibited mild drowsiness. The blood urea nitrogen was elevated mildly as was bromsulphalein test.

Posttreatment ocular findings. The patient's visual acuity at the time of discharge was 20/40 right eye with no change in the visual field. He was discharged on steroids and vasodilators. The lesion revealed activity at the end of one month. The lesion was quiescent eight months later; the visual acuity was 20/200, and a large, dense central scotoma (2/1000 white) was present. The lesion exhibited extensive scarring. The complement fixation test now was negative.

Case 2

Hospital number, 869333. A woman, aged 43 years,

a resident of Ohio, had active central chorioretinitis, right eye; inactive central chorioretinitis, left eye. Visual acuity was 20/200 right eye and 20/200 left eye. The visual fields revealed a large central scotoma (2/1000 white).

Uveitis survey. The histoplasmin skin test was positive; the histoplasma complement fixation test was positive 1:8; the chest film showed evidence of old inflammatory pulmonary disease.

Therapy consisted of 0.5 gm. of amphotericin B in 10 equally divided doses given over an interval of 17 days.

Therapeutic side-effects. Temperature spiking, anorexia, nausea, headache and chills. Mild elevation of the blood urea nitrogen, increased bromsulphalein retention, and a minimal fall in the hematocrit reading. All findings reverted to normal upon cessation of therapy.

Posttreatment ocular findings. The visual acuity was: R.E., counting fingers at three feet and L.E., 20/200. The patient was discharged on Medrol and vasodilators. A large central scotoma 2/1000 white, was present in both eyes. The lesions in both eyes presented a gliotic, slightly elevated scar with minimal pigment migration.

CASE 3

Hospital number, 912574. A man, aged 40 years, a resident of Ohio, had an active perifovealor chorioretinitis and a nongranulomatous iridocyclitis in the right eye; the visual acuity was 20/20 in both eyes; visual field presented a large perimacular scotoma 2/1000 white in the right eye.

Uveitis survey. A positive histoplasmin and tuberculin skin test were obtained. Chest X-ray films revealed pulmonary calcification. The histoplasmin complement fixation test was 1:16 (three months after initiation of therapy).

Treatment consisted of 0.5 gm. of amphotericin B in 10 equally divided doses given over an interval of 14 days: Meticorten (15 mg., q.i.d.) and atropine and Neo-deltacortef drops; Isoniazid (100 mg., three times a day).

Therapeutic side-effects. The patient experienced dizziness, drowsiness and temperature spiking.

Posttreatment ocular findings. The visual acuity was 20/15, right eye, and 20/20, left eye, three months after discharge. No activity was noted and only minimal pigment mottling was observed in the area of the original activity. No scotoma was demonstrable.

CASE 4

Hospital number, 862730. A man, aged 44 years, a resident of Michigan, had active central chorioretinitis, right eye; inactive central chorioretinitis, left eye. The visual acuity was 20/20-1, right eye, and 20/50-2 (eccentric), left eye. The visual fields presented a small central scotoma ½/1000 white right eye and a dense small central scotoma 18/1000 white, left eye.

Uveitis survey. A positive histoplasmin skin test. The chest X-ray films presented equivocal evidence of old inflammatory disease. The histoplasma complement fixation test was positive, 1:8.

Therapy consisted of 0.5 gm. of amphotericin B in 10 equally divided doses given over a 10-day period. Thiamin chloride and nicotinic acid was administered. Decadron 1.0 mgm. was given orally every six hours for a period of two weeks and then slowly tapered.

Therapeutic side-effects. The patient experienced spiking fever, headache, chills, anorexia and back pain.

Posttreatment ocular findings. The visual acuity was 20/20, right eye, and 20/50-2, left eye; the ophthalmoscope revealed only pigment clumping in the macular area left eye; the lesion was quiescent. Complement fixation test reverted to negative.

CASE 5

Hospital number, 914889. A woman, aged 42 years, a resident of Michigan, showed disseminated old chorioretinitis, both eyes; active central chorioretinitis, left eye; the vitreous was very cloudy in the left eye. The corrected visual acuity was 20/20, right eye, and 20/70, left eye. The left eye presented a temporal hemianopic defect including the fixation area on visual field examination.

Uveitis survey. A positive histoplasmin skin test. The chest X-ray film revealed calcium changes typical of old histoplasmosis and a complement fixation of 1:8.

Therapy consisted of 0.7 gm. of amphotericin B in 14 divided doses over a period of 17 days. The patient had been treated prior to her admission with steroids and Isoniazid by her local physician.

Therapeutic side-effects. The patient experienced headache, nausea, backache, chills, spiking fever, diapharesis, and a mild elevation of the blood urea nitrogen.

Posttreatment ocular findings. The vitreous haze cleared in the left eye and a hemispherical raised lesion suggesting a malignant melanoma was observed. P^{32} uptake studies were positive. Visual acuity was 20/100 and the visual field was unchanged. Enucleation was performed and pathologic study revealed a spindle cell type A malignant melanoma of the choroid perforating the sclera along the vortex veins. Culture for Histoplasma capsulatum was negative. The histoplasmin complement fixation test was 1:16 three months after enucleation.

CASE 6

Hospital number, 880626. A man, aged 35 years, a resident of Michigan, had an active central chorioretinitis in the right eye; the left retina was normal. The corrected visual acuity was 20/30 right eye and 20/20 left eye. The visual fields revealed a small central scotoma 1/1000 red right eye.

Uveitis survey. A positive histoplasmin skin test, a positive histoplasma complement fixation test (1:8) and a chest X-ray film presenting calcified nodes and scattered bilateral pulmonary calcification and

scarring suggestive of histoplasmosis were obtained.

Therapy. The patient received 0.5 gm. of amphotericin B in 10 divided doses over a 10-day interval. Nicotinic acid, thiamin chloride and Medrol (2.0 mg., twice daily) were also used.

Therapeutic side-effects. The patient experienced spiking fevers, chills and diaphoresis.

Posttreatment ocular findings. At the time of completion of treatment the visual acuity was 20/20 and a small pericentral scotoma (1/1000 red) was present. The patient was continued on small doses of steroids for three months following discharge. The visual acuity was 20/70, right eye, three months after treatment and 20/80 five months later. The lesion showed no activity at the latter time.

Case 7

Hospital number, 888023. A woman, aged 22 years, a resident of Michigan, had an active central chorioretinitis in the left eye; no pathologic alteration was seen in the right eye. The corrected visual acuity was 20/15, right eye, and 20/60, J11, left eye. The visual field presented a large central scotoma in the left eye 1/1000 white.

Uveitis survey. A positive histoplasmin and tuberculin skin test, a negative histoplasma complement fixation test, and a chest X-ray film compatible with old inflammatory disease of the chest were secured.

Therapy consisted of 1.0 gm. of amphotericin B administered in 20 divided doses over a 20-day interval. In addition typhoid H antigen, thiamin chloride, and nicotinic acid were employed.

Therapeutic side-effects. The patient experienced mild anorexia, nausea, diarrhea, tmeperature spiking and malaise.

Posttreatment ocular findings. The fundus showed less activity. The visual field and acuity of the left eye remained the same immediately following treatment. One year after completion of treatment the lesion was quiescent and the visual acuity was counting fingers at three feet.

Case 8

Hospital number, 734820. A woman, aged 23 years, a resident of Michigan, had an acute exacerbation of an old central chorioretinitic lesion in the left eye; the ocular findings in the right eye were negative for pathologic changes. The visual field presented a small pericentral scotoma (1/1000 red). The corrected visual acuity was 20/20-1 in each eye.

Uveitis survey. A positive histoplasmin skin test, a negative complement fixation test and chest X-ray findings previously diagnosed as histoplasmosis (1957) were obtained.

Therapy consisted of 0.35 gm. of amphotericin B in seven equally divided doses over seven days.

Therapeutic side-effects. The patient experienced chills, fever, nausea, vomiting, headache, and depressed platelet count. The drug was stopped because of decreased hemoglobin and increased blood urea nitrogen. No further medication was given when the complement fixation test was read as negative for histoplasma.

Posttreatment findings (ocular). The ocular findings were much as before treatment except less vitreous haze was noted and the activity was less. The visual acuity was 20/20-1 in both eyes.

Case 9

Hospital number, 760450. A woman, aged 39 years, a resident of Michigan, had an acute central chorioretinitis in both eyes. The corrected visual acuity was 20/30, right eye, and 20/80, left eye. The visual fields exhibited a paracentral scotoma in the right eye (2/1000 red) and a large central scotoma in the left eye.

Uveitis survey. The patient exhibited a very positive histoplasmin and mildly positive tuberculin skin test. The chest film was negative and the histoplasma complement fixation test was negative.

Therapy. The patient had received streptomycin, para-amino-salicylic acid and Isoniazid for several months without result. Amphotericin B, 0.5 gm in 10 divided doses over a 11-day period, was administered. Decadron was also employed.

Therapeutic side-effects. The patient experienced headaches, abdominal cramping, spiking fever, chills, phlebitis (intraveous, arm), lethargy, diaphoresis and an elevated blood urea nitrogen.

Postreatment ocular findings. The visual acuity improved to 20/25 in the left eye and decreased to 20/50 in the right eye. The lesion was quiescent in the left eye but continued to exhibit activity in the right eye as late as five months after therapy.

Comment

All of the nine cases presented exhibited a positive skin test to histoplasmin but only six of these demonstrated a significant positive Histoplasma complement fixation titer. The nine patients thus fall into two groups: (1) those presenting a positive histoplasmin skin test and a positive Histoplasma complement fixation test (Cases 1-6) and (2) those presenting only a positive histoplasmin skin test (Cases 7-9). Little response to amphotericin B therapy was encountered in the latter group. The former group (Cases 1-6), however, deserve closer scrutiny since the positive Histoplasma complement fixation test suggests activity of the disease. In the group of six patients two (Cases 3 and 4) demonstrated objective improvement in visual acuity and fields; two poorer visual acuity (Cases 1 and 2) but subsidence of activity of the lesions, and one patient (Case 5) had the diagnosis altered (malignant melanoma) after sufficient improvement in

the vitreous haze resulted to permit more accurate visualization. One case (6) had the same visual acuity immediately after treatment but this deteriorated later while on steroid therapy despite quiescence of the chorioretinitis.

Ideally, only those cases in which one can obtain serologic evidence of active histoplasmosis should be treated with amphotericin B. This was not done in our cases since it was not thought, at first, expedient to wait for the complement fixation test results. It is amazing that six of the nine cases actually did exhibit, eventually, a positive Histoplasma complement fixation test. It is evident that a certain number of patients with active chorioretinitis and only a positive histoplasmin skin test will receive ill-advised therapy. Through experience we feel strongly that since amphotericin therapy is an expensive, rigorous, and dangerous therapy it should not be instigated unless strong presumptive evidence of histoplasmosis activity is available to the physician!

Since several of the patients, including Cases 3 and 4, received steroid therapy in conjunction with the administration of the amphotericin B it is freely admitted that it was impossible to determine to what degree the latter agent was responsible for the clinical observed subsidence. It is regrettable that steroids were employed but their utilization was dictated by threatened destruction of the macular area. It is to be pointed out, however, that, in our experience, a certain number of such cases treated solely with long-term steroid administration continued to exhibit activity and on occasion the chorioretinitis would actually exacerbate, leading to phthisis. It would be, of course, most desirable to obtain a series of cases presenting peripheral chorioretinitis in patients manifesting presumptive evidence of histoplasmosis and treated with amphotericin B alone. Such a series would possibly answer many of the questions which this study cannot.

Amphotericin B therapy, as previously emphasized, is not an innocuous regimen. A survey of the complications encountered in the nine reported patients revealed the following significant signs and symptoms: (1) spiking fever (eight out of nine); (2) chills (six out of nine); (3) elevated blood urea nitrogen (five out of nine); (4) headache (five out of nine); (5) nausea (four out of nine); (6) anorexia (three out of nine); (7) dizziness (three out of nine); (8) drowsiness (three out of nine); (9) diaphoresis (three out of nine); (10) increased bromsulphalein (two out of nine), and (11) decreased hemoglobin, platelet count phlebitis and abdominal pain (one out of nine). (The majority of the latter signs and symptoms occurred in one patient (Case 8) and necessitated cessation of therapy which was not resumed when the Histoplasma complement fixation test was reported as negative.)

These reactive signs and symptoms returned to normal in all nine cases following cessation of treatment and no detectable evidence of permanent deleterious effect to any organ or system has been found. Christie's evidence that sulfonamide therapy is of specific value in the management of systemic histoplasmosis should stimulate its use in cases of chorioretinitis. As a result of our experience with amphotericin B and motivated by Christie's report employing sulfonamides the following therapeutic regimen of suspected cases of histoplasmosis chorioretinitis is suggested:

a. A careful medical survey of the patient, particularly ruling out nephritic, hepatic and hematopoietic pathology.

b. Intravenous amphotericin B in five-percent glucose utilizing 1.0 mg. per kg. of body weight, not to exceed 75 mg., usually 50 mg., per administration. Daily or alternate daily injection may be employed depending upon the patient's systemic response to the drug. A total of 1.0 gm. of the drug should be used.

c. During the interval of therapy the kidney, liver and bone-marrow function should

be carefully followed. This may be done by alternate daily blood urea nitrogen, hematocrit, white blood count and cellular differentiation determinations. Bromsulphalein retention and phenolsulfonphthalein clearance studies should be obtained weekly. A blood urea nitrogen greater than 30 mg. percent or evidence of moderate hepatocellular or bone marrow depression should dictate cessation of therapy. Should these findings return to normal therapy may then be re-instituted.

In an attempt to minimize side-effects of the drug the following ancillary regimen may be employed: Phenergen (25 mg. by mouth) and acetyl salicylic acid (10 gr. by mouth) three hours prior to intravenous administration of amphotericin B and repeated every three hours as necessary. In recalcitrant cases benadryl (50 mg.) may be mixed with the intravenous preparation.

d. Steroid therapy is to be administered only when macular or ocular destruction is imminent.

e. Sulfadiazine (1.0 gm. four times a day) should be started seven days prior to cessation of amphotericin B infusions and continued on a long-term basis with or without steroids when the patient is discharged from the hospital. Repeated careful urinalyses must be performed in association with this dosage of sulfonamides and in addition the patient should be warned to maintain a high fluid intake.

This paper has not established, other than on speculative and presumptive evidence, that histoplasmosis affects the eye. The presence of an active chorioretinitis associated with: (1) a positive Histoplasmin skin test, (2) a positive histoplasma complement fixation test, (3) roentgenographic evidence of pulmonary histoplasmosis, and (4) the absence of other causative factors is, however, as good or better evidence than is usually available to implicate other granuloma-causing agents. Histoplasma capsulatum has not been recovered from ocular tissues, but when consideration is accorded to the widespread involvement of other body tissues and organs by this agent it seems extremely plausible that the eye may likewise be affected.

Considerable debate is occurring as to the significance of a Histoplasma complement fixation test positive in 1:8 dilution. At present many authorities consider this as positive evidence of active disease. Further clinical correlation, however, is required.

The penetrability of amphotericin B into the human eye is still unproven and before one can definitely assign ocular therapeutic properties to this drug this problem must be answered. Since amphotericin B has been detected in the cerebrospinal fluid it might be postulated that it can also appear in the aqueous. Sery and Montana[28] found no evidence of such penetration into the anterior chamber of rabbits no matter what the route of administration, but studies related to levels of the drug in the coats of the eye have not been obtained.

It is apparent that this paper had produced no confirmatory evidence that ocular histoplasmosis is an entity. The paucity of treated cases, the short period of follow-up, the high incidence of destructive scarring of the involved retina and observed exacerbation of the lesion in several cases leaves much to speculation as to the efficiency of amphotericin B in the treatment of the reported cases. Suffice it to say that an agent, successful elsewhere in treating systemic histoplasmosis has been employed in the therapeusis of certain cases of chorioretinitis. It appeared, with and without the use of steroids, to effect quiescence of the chorioretinitis. Further experience and study are apparently necessary to answer the numerous questions that have evolved with the use of the drug.

Summary

Nine selected cases of chorioretinitis, presumably Histoplasma capsulatum in causation, were subjected to amphotericin B therapy with and without steroid supplement. Subsidence of the chorioretinitis activity re-

sulted in most cases. Systemic reactions to amphotericin B were encountered and were summarized. These drug reactions produced no permanent sequelae but were alarming and left no doubt that the drug is not innocuous, but rather one that requires the most meticulous care in its administration.

Conclusion

Amphotericin B, an antibiotic with proven antifungal activity, has been successfully employed in the treatment of systemic histoplasmosis. The results of its employment in the treatment of selected cases of chorioretinitis, although far from striking, suggest that further trial of the drug in cases of suspected histoplasmosis of the eye is warranted.

University Hospital

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NONPERFORATING EYE INJURIES WITH HYPHEMA*

MORRISS M. HENRY, M.D.
Fort Smith, Arkansas

A patient who has a contusion of the eye with hyphema will often be given a guarded prognosis by many experienced oculists because complications are frequent, even when the amount of blood in the anterior chamber is small and the injury appears slight. To determine the incidence of complications and the prognosis when complications occur, the records on traumatic hyphema from the Massachusetts Eye and Ear Infirmary and the Massachusetts General Hospital were reviewed from 1947 to 1958.

Table 1 is an analysis of 204 cases that were seen within 24 hours of the injury. Only those cases admitted to the hospital within 24 hours of the initial injury are included, since a number of the patients that came in after 24 hours were referred to the hospital after complications had become evident. Table 1 lists the injuries or complications that may occur and the number of times this was found. One or more lesions may be present in the same eye.

One of the more common complications following nonperforating injuries is a cataract which occurred in 11 percent of the cases studied. The cataract is not always evident on the initial examination and may not begin to appear until five to 10 days after the injury. A number of the cataracts became stationary after varying periods of time and some of the eyes maintain good vision despite the lens opacity.

Injury to the choroid and retina occurred in 14 percent of the cases and this also may not be evident on the initial examination. The macula is the area that most frequently shows the injury and usually this impairment of vision is permanent.

Vitreous hemorrhage is another of the more common complications in eyes with traumatic hyphema. Visual acuity is often reduced to light perception or hand motion. Several such cases returned to 20/20 vision after having only light perception for several months.

A second hyphema occurred in 17 percent

TABLE 1

ANALYSIS OF 204 CASES SEEN WITHIN 24 HOURS OF THE INJURY*

Number of eyes that had an uncomplicated course with a return of good vision	105	
Number of eyes that developed some complication	99	(49%)
Complications		
Secondary hyphemas	35	(17%)
Glaucoma		
a. occurring at time of initial injury	13	
b. associated with secondary hyphema	18	
c. occurring later	10	
	41	(20%)
Tear in Descemet's membrane	1	
Permanent traumatic mydriasis	3	
Iridodialysis	9	
Ruptured iris sphincter	3	
Dislocation of lens	10	
Cataract	22	(11%)
Vitreous hemorrhage	21	(10%)
Chorioretinal edema or injury	28	(14%)
Optic atrophy	1	
Retrobulbar hemorrhage	1	
Hematogenous pigmentation of cornea	1	
Number of eyes with good final visual acuity	169	(83%)
Number of eyes with poor final visual acuity	35	(17%)

* One or more lesions may be present in the same eye.

* This paper was presented before the Massachusetts Eye and Ear Infirmary alumni meeting, April 14, 1959.

TABLE 2

DAYS THE SECOND HEMORRHAGE OCCURRED

Day	2	3	4	5	6	7	8	9	10
Number of Eyes	29	26	15	7	4	2	1	1	0

of the cases in this series. It is apparently very difficult to anticipate which of the eyes will develop this complication. Some of the eyes with only a small initial hyphema and little or no other visible evidence of injury developed a second hyphema. In about one half of the eyes that have a second hyphema the blood fills the anterior chamber and changes from a bright red to a black color with a marked elevation in the ocular tension.

The question as to what are the days most likely for the second hyphema to occur may be best answered by listing the day on which it occurred. Some of the eyes bled several times and are listed on more than one day.

Activity apparently plays a part in second hyphemas. It was noted on at least seven occasions that the hemorrhage occurred when the patient got up and moved about on the second to fifth day.

Most of the patients admitted to the hospital were treated with bedrest and double eye patching; 137 patients did not receive any local medication. Despite this, 21 (13 percent) of these cases developed a second hyphema. There were 52 cases in which mydriatics were used along with the bedrest and eye patching. Six (12 percent) of the cases developed a second hyphema. Twice when the mydriatic was used for the first time several days after the injury a second hemorrhage occurred, one as late as the fifth day.

Treatment of the glaucoma in the second hyphemas was usually by Diamox and miotics. Surgery was resorted to when it became evident that medications would not control the the tension.

The surgical procedure used by each surgeon was governed to some extent by the appearance of the second hemorrhage and the severity of the glaucoma. In five eyes paracentesis was used in an attempt to control the tension. In two of these five cases the incision was made large enough to irrigate the anterior chamber and instill an air bubble. This worked well in these two cases. Of the three remaining eyes, one had an anterior chamber one-half filled with blood and this responded well to the paracentesis. In the other two cases only a small opening was made with a Wheeler knife to relieve the high tension. These two eyes required repeated paracenteses but in neither case did this work for very long and an attempt was later made to evacuate the clot. If the tension was very high and the anterior chamber was completely filled with a black clot the surgeon usually elected to evacuate the clot as the initial procedure. This was done in a manner similar to removing a cataract. A conjunctival flap was turned back and some form of preplaced suture was used. The anterior chamber was entered with either a keratome or a Wheeler knife and attempts were made to dislodge the clot with saline irrigation. The iris would sometime prolapse into the wound and require excision. A serious complication was fresh bleeding at the time of the operation, or in a few days following the operation. Two of the five eyes that continued to bleed following the operation required enucleation. The clot would sometimes be found to be firmly attached to the iris and adjacent structures and too vigorous an effort in removing the clot would sometimes result in damage to the eye.

Seventeen percent of all the patients with traumatic hyphema in this series have a final vision of 20/40 or less. This was usually the result of injury to the lens or macula. If the eye developed a second hyphema the chances of having poor vision moved to 28 percent.

When surgery becomes necessary for the glaucoma, the prognosis looks grim indeed. However, this is not always the case. Sixty-two percent of the eyes requiring surgical intervention for the glaucoma had a final vision of better than 20/40.

The majority of nonperforating eye injuries in this series were due to thrown objects such as rocks, pieces of wood, or balls by boys between five and 15 years of age. Despite the fact that the BB gun has been outlawed in Massachusetts since 1950, it is still a common cause of eye injuries. Industrial accidents make up a surprisingly small percentage of the total number of eye injuries in this series.

Conclusions

1. Approximately 50 percent of the eyes that receive a blow severe enough to cause a hyphema will show some injury to the eye other than the hyphema.

2. Permanent impairment of vision to 20/40 or less occurred in 17 percent of the cases of traumatic hyphema in this series.

3. The major causes for the permanent loss of vision are cataracts and chorioretinal injury.

4. One of the most frequent complications is a second hyphema and this occurred in 17 percent of the cases in this series. About one half of the eyes with a second hyphema develop acute congestive glaucoma. This type of glaucoma does not respond to medical therapy in most cases. Surgical removal of the clot or part of it within 24 to 48 hours to relieve the glaucoma apparently offers a relative good prognosis. A good visual outcome was obtained in 62 percent of the cases treated surgically.

5. The surgical incision should be made large enough for the clot to be removed in one piece and to give adequate exposure of the anterior chamber. This usually requires an incision as large as one used for an intracapsular cataract extraction.

6. The second hyphema occurs most commonly in the first four days following the injury. The relationship of activity to a second hyphema occurs too frequently to be considered due to chance. The physician who insists on strict bedrest and double eye occlusion for five days in an attempt to prevent a second hyphema is using sound judgment in his treatment of the case.

7. Dilating the pupil with a mydriatic did not alter the occurrence of a second hyphema in the cases in this series. On several occasions when the mydriatic was used for the first time several days after the injury a second hyphema developed.

602 Garrison Avenue.

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THE ECHOGRAM IN VITREOUS OPACITIES*

ARVO OKSALA, M.D.
Jyväskylä, Finland

In several earlier studies of mine, part of which were made in collaboration with A. Lehtinen[3–6, 8, 9] I have been able to observe that vitreous opacities, for example, formation of fibrous tissue, exudation and hemorrhages, can often trace reflections on the scale of an ultrasonic equipment. Baum and Greenwood[1, 2] have used later a much more complicated and expensive amplitude modulation technique with a scanning system, and made identical observations.

Up to the present and for a period of over three years, I have studied dozens of cases of disease and trauma with vitreous opacities by the aid of an ultrasonic apparatus. Since I have not previously reported these experiences in more detail and since the literature on the subject has so far been restricted to the above-mentioned studies, I shall describe below, in the light of some typical cases, my present conception on the possibilities of use of an ultrasonic equipment for diagnosing vitreous opacities.

A. RESEARCH EQUIPMENT AND TECHNIQUE

In all my investigations I have used the ultrasonic apparatus of Dr. J.u.H. Krautkrämer, Gesellschaft für Elektrophysik, Köln, West Germany, which has been described in some previous studies of mine.[3, 7] The crystal I used was a barium titanate crystal of five-mm. diameter and 6.0 Mhz, which was plated with silver and specially constructed for ophthalmologic diagnosis. The crystal has also been previously described.[3, 4] In all my investigations the ultrasonic impulse power was five and amplification 10. Thus the maximum effect of the apparatus was used.

For the examination the eye was anesthetized with three-percent Cornecain (Hoechst) drops, and thereafter two drops of a one-percent methylcellulose solution which served both as sound transmitter and formed a protective film between the crystal and the eye surface, were pipetted into the eye. The examination was usually conducted without a blepharostat. The crystal was then lightly pressed by hand against the eye. By changing the place and direction of the crystal it was possible to examine the whole vitreous. The necessary photographs were taken of the tracings which appeared on the scale of the ultrasonic equipment.

B. ECHOGRAMS IN VARIOUS VITREOUS OPACITIES

1. VITREOUS HEMORRHAGES

CASE 1

A man, aged 61 years, into whose left eye a metal sliver had flown on the day before coming for treatment, as he was hammering on a chisel.

Eye examination, October 14, 1958. Vision was: O.D., 0.8; O.S., 0.02. The right eye was sound. In the left eye a perforated wound was seen on the margin of the cornea, and a small hole in the corresponding place of the iris. The lens was transparent. An extensive hemorrhage was seen in the vitreous both by ophthalmoscope and a slitlamp. Roentgenologic examination revealed that the iron sliver had penetrated through the globe and was lodged deeply in the orbit.

Ultrasonic examination, October 15, 1958. This examination was carried out both for an elucidation of the extent of the hemorrhage and of the condition of the fundus behind it. In Figure 1 we can see a typical echogram at the time the sound spurt passed through the hemorrhage. On the left there is a high initial impulse or initial echo which does not find sufficient space on the screen. It is followed by the zero-line of the undamaged vitreous until, in the place marked by arrows, the echoes reflected by the border surfaces of the vitreous and the hemorrhage can be seen. On the right echoes are visible which have been given off by the fundus and the retrobulbar tissue. A zero-line is obtained between the hemorrhage and the fundus. No echo suggesting detachment of retina is seen.

CASE 2

A man, aged 32 years, who had an attack of nausea two days before. After vomiting the patient noted a

* From the Ophthalmic Department of the Central-Finland Regional Hospital.

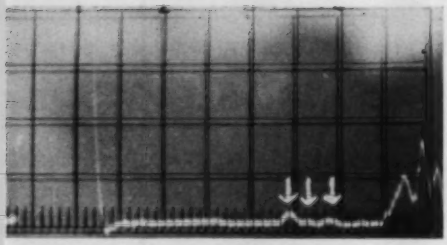

Fig. 1 (Oksala). Echogram in Case 1. On the left a high initial echo does not find enough space on the screen. It was followed by the zero-line of an undamaged vitreous, until three echoes are seen, emitted by the hemorrhages and marked by arrows. They are followed by a short zero-line. On the right echoes reflected by the fundus and the retrobulbar tissue.

sudden deterioration in the visual acuity of the right eye.

Eye examination, April 20, 1959. Vision was: O.D., 0.02; O.S., 1.0. The left eye was sound. No injection was seen in the right eye and its anterior parts were free of symptoms. Both ophthalmoscopy and biomicroscopy showed in the region of the macula in the right fundus an extensive preretinal hemorrhage which had descended in the manner of a hyphema.

Ultrasonic examination, April 21, 1959. The object of the research was to throw light on the position of the retina behind the hemorrhage. Figure 2 shows one of the echograms obtained, from which it emerges firstly that the hemorrhage was unmistakably in front of the retina, secondly, that there was some vitreous between it and the retina, and thirdly that the retina was not detached. The arrow on the photograph marks the echo reflected by the hemorrhage. Immediately behind it is the echo emitted by the posterior eye wall.

Case 3

A man, aged 48 years, who 10 years before had had retinal periphlebitis in both eyes. One day before coming up to our Ophthalmic Department the patient noted sudden deterioration of the vision in his left eye.

Eye examination, April 29, 1959. Vision was: O.D., 1.0; O.S., 0.06. In the right fundus some obliterated veins were seen and around them atrophic chorioretinal patches. No injection was visible in the left eye and its anterior parts were asymptomatic. On the other hand, there was a circumscribed hemorrhage in the anterior vitreous behind the lens. No hemorrhages were found in the fundus.

Ultrasonic examination, April 29, 1959. Figure 3 illustrates one of the echograms obtained in this case. A high initial echo is again seen on the left. The lower echo which follows it is reflected from the posterior surface of the lens. A still slighter echo marked by the arrow comes from the border surface between the vitreous and the hemorrhage. The echo from the posterior eye wall seen on the right is very low, because the sound waves do not encounter it perpendicularly. The posterior part of the vitreous produced a normal zero-line in all directions examined. Thus the ultrasonic examination showed in the first place that there was no retinal detachment, and in the second, that no hemorrhages, at least no fresh ones, were present in the posterior part of the vitreous.

Comment

In the first case the vitreous hemorrhage was due to trauma, in the second to an unknown cause and in the third probably to retinal periphlebitis. In every case the hemorrhage was fairly extensive and still clearly circumscribed at the time when the ultrasonic examination was performed. In each case the ultrasonic examination produced on the scale, a clear echo from the border surface of the vitreous and the hemorrhage. This examination made it possible to determine the position of the retina even behind

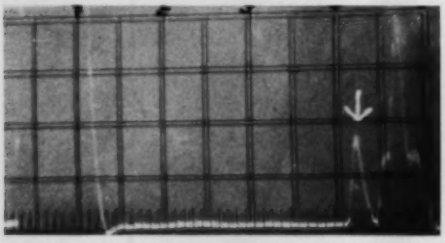

Fig. 2 (Oksala). Echogram in Case 2. The arrow points to an echo given off by a hemorrhage which is closely in front of the retina. The echo of the fundus on this photograph is much higher than on the foregoing Figure 1.

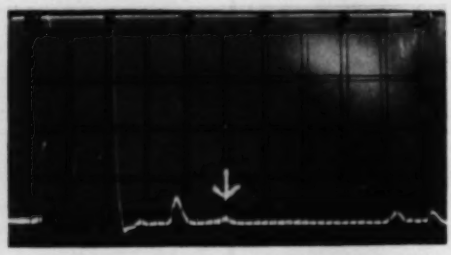

Fig. 3 (Oksala). Echogram in Case 3. The arrow points to the echo emitted by the hemorrhage. The echo between this and the initial echo is given off by the posterior surface of the lens.

the hemorrhage, and in addition to assess with a high degree of certainty whether other fresh hemorrhages than those seen in ophthalmoscopy were present in the vitreous.

2. Vitreous opacities in exudative uveitis

Case 4

A woman, aged 36 years, whose vision of the left eye began to deteriorate slowly a fortnight before her admission to our Ophthalmic Department. She gave a history of previous health.

Eye examination, February 9, 1958. Vision was: O.D., 1.0; O.S., 0.15. The right eye was sound. Strong ciliary injection was present in the left eye. The cornea showed some slight precipitates. Pronounced aqueous flare was found in the anterior chamber. The iris was hyperemic and three posterior synechias were visible in it. The lens appeared transparent. The vitreous showed numerous bandlike opacities which undulated together with the movements of the eye. The fundi, which indeed were poorly visible, revealed no pathologic changes. Our diagnosis was acute iridocyclitis. We were unable to clarify the etiology.

Ultrasonic examination, February 10, 1958. This examination produced numerous slight echoes from the vitreous in the echogram on the screen; their position and height varied slightly according to the direction of investigation and to movements of the eye. Figure 4 illustrates a typical echogram which shows four echoes emitted by the vitreous opacities (arrows). The echogram did not reveal any other pathologic changes.

Case 5

A girl, aged 16 years, previously completely healthy. Three days before there was an onset of pain and redness in the right eye and the vision deteriorated.

Eye examination, February 26, 1958. Vision was: O.D., 0.25; O.S., 1.0. The left eye was sound. The right eye showed pronounced ciliary injection. Numerous small precipitates were present on the cornea. Strong aqueous flare was seen in the anterior chamber. The iris was hyperemic. Several bandlike opacities oscillated in the vitreous. The fundus seemed normal. Again our diagnosis was acute iridocyclitis. The etiology remained obscure.

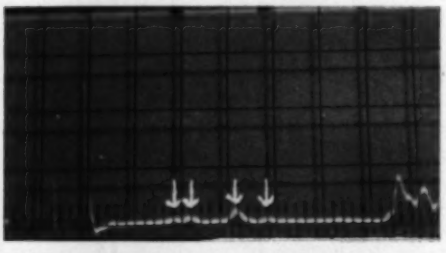

Fig. 4 (Oksala). Echogram in Case 4. The arrows mark four echos reflected by vitreous opacities of exudative uveitis.

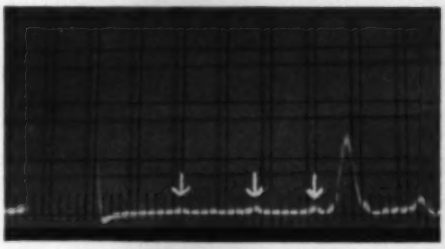

Fig. 5 (Oksala). Echogram in Case 5. The arrows point to three echoes reflected by vitreous opacities of exudative uveitis. The higher echo on the right is emitted by the fundus.

Ultrasonic examination, Feburary 26, 1958. The vitreous produced in different echograms numerous low echoes whose position and height showed slight variations. In Figure 5 we can see three such echoes reflected from inflammatory opacities of the vitreous. No other pathologic features were seen on the echogram.

Case 6

A man, aged 23 years, whom we had treated one year before with a diagnosis of chronic tuberculous uveitis of both eyes. At the time the patient was given for four months antituberculosis treatment (streptomycin + PAS + INH), under which the uveitis was clinically completely cured. On the day before entering our Ophthalmic Department the patient noted a large moving shadow in the visual field of the left eye.

Eye examination, April 21, 1959. Vision was: O.D., 0.60; O.S., 0.25. No injection was seen in the right eye. The anterior chamber of the right eye was transparent. In the posterior capsule of the right lens there was a central opacity. The right vitreous and fundus had a healthy appearance. Slight ciliary injection was seen in the left eye. The cornea showed some precipitates and slight aqueous flare in the anterior chamber. Slight hyperemia and two posterior synechias were seen in the iris. A large dense opacity cloud was seen in the middle of the vitreous both with ophthalmoscope and with a slitlamp. The fundus appeared normal. It was obvious that previous tuberculous uveitis had recurred in the left eye.

Ultrasonic examination, April 21, 1959. Nothing pathologic was seen on the echogram of the right eye. In the echogram of the left eye the echo emitted by the large vitreous opacity was clearly visible in several directions of investigation. It is seen on Figure 6 marked by the arrow. In the same photograph the lower echo immediately following the initial one was given off by the posterior surface of the lens.

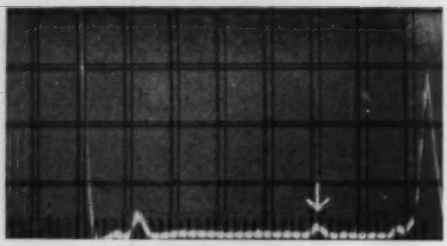

Fig. 6 (Oksala). Echogram in Case 6. This photograph shows only one echo produced by the vitreous opacity in a case of exudative uveitis (arrow). The low echo behind the initial one is reflected from the posterior surface of the lens.

Comment

In all three cases described here the vitreous opacities produced by exudative uveitis could be seen on the echograms as well. In two cases several echoes from the vitreous opacities were visible, whereas in the third there was only one opacity of the vitreous which produced an echo. Ophthalmoscopic, biomicroscopic and ultrasonic observations were fairly consistent with each other.

3. Vitreous abscess

Case 7

A man, aged 34 years, into whose left eye an iron sliver flew on October 25, 1957, while he was working with a hammer. The patient did not come to our Ophthalmic Department before October 28, 1957. The iron sliver which had penetrated into the vitreous was removed on the following day by means of a magnet. The patient was given considerable amounts of penicillin both subconjunctivally and intramuscularly. At first the eye recovered rapidly, and the patient was discharged for home treatment. On December 19, 1957, the patient re-entered our department, because the left eye had begun to pain him. It had become blind.

Eye examination, December 19, 1957. Vision was: O.D., 1.0; O.S., 0. The right eye was sound. The left eye revealed strong ciliary injection. Hypopyon was present in the anterior chamber, and the iris was highly hyperemic. The lens appeared transparent. The vitreous showed a yellowish gleam through the pupil. Our diagnosis was suppurative panophthalmitis and vitreous abscess, which could later be verified after the enucleation of the eye.

Ultrasonic examination, December 20, 1957. On every echogram from the left eye one could see in the middle of the zero-line of the vitreous a clear but fairly low echo, which is illustrated in Figure 7 marked by the arrow. On either side of this echo one could distinguish now and again very low echoes.

Case 8

A boy, aged seven years, whose left eye was pierced four days before by a haw thorn.

Eye examination, October 22, 1958. Vision was: O.D., 1.0; O.S., hand movements. The right eye was sound. The left eye showed strong ciliary injection. Hypopyon was seen in the anterior chamber. The iris was hyperemic. The vitreous shone yellowish through the pupil. In spite of copious antibiotic administration over a time of three weeks (penicillin, Chloromycetin) no improvement of the vitreous could be achieved. Our diagnosis was suppurative panophthalmitis and vitreous abcess, which could be verified after enucleation of the eye.

Ultrasonic examination, October 26, 1958. In this examination one could again see on each echogram in the region of the vitreous one clear echo, which is marked by an arrow in Figure 8. Now and then some very slight echoes were seen on either side of this echo. No other pathologic features were seen on the echogram.

Case 9

A girl, aged 11 years, who right eye was struck by an iron wire two weeks before coming for treatment. Since the patient could see well at first, and redness and pain remained absent for several days, the parents failed to bring the patient for treatment in time.

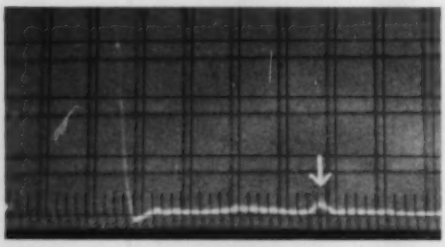

Fig. 7 (Oksala). Echogram in Case 7. The arrow marks the echo reflected by the vitreous abscess. The echo from the fundus is not seen on this photograph.

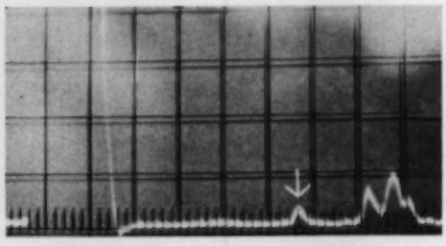

Fig. 8 (Oksala). Echogram in Case 8. The arrow marks the echo reflected from the vitreous abscess; on either side of it a zero-line.

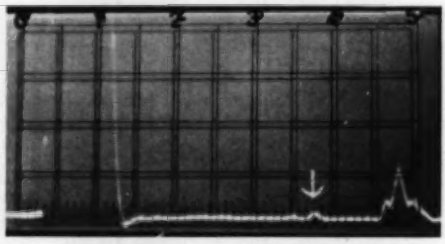

Fig. 9 (Oksala) Echogram in Case 9. The arrow marks the echo reflected from the vitreous abscess.

Eye examination, May 10, 1959. Vision was: O.D., 0; O.S., 1.0. The left eye was sound. In the upper lid of the right eye as well as in the sclera, at about 10 mm. from the limbus, there was a scar from a perforation wound. The eye showed strong ciliary injection. Hypopyon was present in the anterior chamber. The iris was hyperemic. The vitreous showed a yellow gleam through the pupil. In spite of intense antibiotic medication of two weeks' duration, the vitreous failed to improve. Enucleation of the eye was made on May 25, 1958, and our diagnosis of suppurative panophthalmitis and vitreous abscess could be verified.

Ultrasonic examination, May 16, 1959. Every echogram showed one clear echo in the area of the vitreous. It is seen in Figure 9 marked by the arrow. Now and then very low echoes could be distinguished on either side of this echo. Otherwise the echograms were normal.

Comment

Very similar echograms were obtained in each of the three cases of vitreous abscess reported by me. The echogram invariably showed in the region of the vitreous one low but marked reflection, on either side of which some very slight echoes could be distinguished now and then. Since the anterior parts of the eye, the cornea, anterior chamber and lens were still fairly transparent in these eyes, the diagnosis of vitreous abscess could be made on the basis of the history as well of the ophthalmoscopic and biomicroscopic examination.

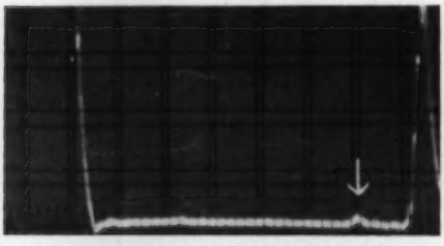

Fig. 10 (Oksala). Echogram in Case 10. The arrow points to the echo given off by fibrous tissue bands in the posterior part of the vitreous.

4. Proliferating retinitis

Case 10

A woman, aged 30 years, who came to our Ophthalmic Out-Patient Department because of acute conjunctivitis. The patient gave a history of trauma to her right eye in her childhood and stated that its vision had remained weak ever since.

Eye examination, December 2, 1957. Vision was: O.D., 0.3; O.S., 1.0. The left eye was sound. In the right eye conjunctival injection could be seen. The cornea, anterior chamber and lens were transparent. The iris was normal. In the posterior part of the vitreous a fibrous band passed in the temporal direction, emerging from the retina and extending close to the macula. Ophthalmoscopy did not reveal any hemorrhages or retinal detachment.

Ultrasonic examination, December 2, 1957. A pathologic echogram was obtained from the right eye only when the sound waves were directed temporally toward the connective tissue in the vitreous. In Figure 10 the arrow marks the echo emitted by this tissue which would sometimes be higher than the one seen on the photograph. The echograms did not reveal any other pathologic features.

Comment

In cases of proliferating retinitis a clear echo is seen reflected on the echogram by the fibrous tissue. The height of the echo is very variable because the fibrous tissue bands can be very dissimilar; whereas the localization of such an echo on the echogram does not greatly change in the same direction of examination.

Discussion

Clear echoes reflected by vitreous opacities could be seen in the echograms of all the cases described by me. However, this is not possible in every case belonging to the disease groups discussed here.

Fresh hemorrhages, even small ones, are nearly always reflected as clear echoes. On the other hand, hemorrhages of several days' standing, when the demarcating line between the healthy vitreous and the hemorrhage has already become more or less diffuse, are more

difficult or impossible to see on an echogram. If the anterior surface of the hemorrhage is extensive and even, and the sound waves encounters it perpendicularly, quite a high echo may be reflected by this surface, as seen in Figure 2.

Among vitreous opacities of exudative uveitis, vitreous abscesses and fibrous tissue bands in proliferating retinitis, only those of highest acoustic density produce echoes which can be registered by our present-day research equipment. A heightening of the frequency of an ultrasonic apparatus would obviously increase the resolving power of the equipment in this respect.

It is usually extremely difficult or even impossible to differentiate between the foregoing vitreous opacities on the basis of the height and shape of the echoes, and such a necessity is only seldom experienced in practice. However, it would perhaps be well to mention that several low reflections usually indicate vitreous opacities of exudative uveitis. Fresh hemorrhages often produce a higher echo, at least in one direction of investigation. Still, it is of more importance to know that the echogram of luxatio lentis, intraocular tumor and a foreign body, as well as retinal and choroidal detachment, can mostly be easily distinguished from the echograms produced by vitreous opacities.

In the assessment of vitreous opacities, the echogram is of great practical significance in those cases in which we are unable to explore the vitreous and the fundus by usual methods of investigation, that is ophthalmoscopy or biomicroscopy, on account of, for example, corneal scars or cataract. If several low echoes are reflected from the vitreous, it frequently indicates that after possible cataract extraction we cannot expect fairly good vision because of vitreous opacities. Simultaneously we can see on the echogram with a high degree of certainly whether the retina is in position and whether a tumor is present in the eye or not.

I feel that an ultrasonic examination is worth while in all severe cases of vitreous opacities. On the basis of the echogram we can sometimes obtain a better idea than with the aid of ophthalmoscopy or biomicroscopy of the density, localization and copiousness of vitreous opacities, as well as of their relation to the fundus.

Summary

In the Ophthalmic Department directed by me I have, for a period of over three years, examined numerous different cases of vitreous opacities with the aid of the echogram. Fresh hemorrhages almost invariably reflect clear echoes. Of the vitreous opacities associated with uveitis, vitreous abscess and fibrous tissue bands in proliferating retinitis, only those with a higher acoustic density are able to emit echoes. Ten typical cases are reported.

Echograms are of great practical significance for the assessment of vitreous opacities in those cases in which we are unable to visualize the vitreous by routine methods of examination, for example, on account of corneal scars or cataract. On the basis of these echograms we can further determine with a high degree of certainty whether the retina is in position and whether or not a tumor is present in the eye.

Central-Finland Regional Hospital.

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USE OF METHAZOLAMIDE (NEPTAZANE) IN THE THERAPY OF GLAUCOMA*

Comparison with acetazolamide (Diamox)

Bernard Becker, M.D.
Saint Louis, Missouri

Carbonic anhydrase inhibitors are useful adjuncts to miotics in the therapy of glaucoma. The partial suppression of secretion induced by systemic carbonic anhydrase inhibitors is of enormous value in the short-term therapy of all varieties of glaucoma, particularly the acute glaucomas. The use of these agents in long-term therapy of the chronic glaucomas proves successful in many instances. The limitations of long-term therapy with available carbonic anhydrase inhibitors (acetazolamide [Diamox], ethoxzolamide [Cardrase], and dichlorphenamide [Daranide]) result more often from intolerance of side-effects than from failure of pressure control. The search continues for carbonic anhydrase inhibitors which will partially suppress aqueous-humor formation but will induce less in the way of systemic side-effects.

Methazolamide is closely related to acetazolamide in structure and it has only slightly greater activity as a carbonic anhydrase inhibitor in vitro.[1] However, it appears to enter the aqueous humor and spinal fluid from the plasma more effectively than acetazolamide, and produces comparable lowering of intraocular pressure in doses approximately one third to one fourth those of acetazolamide. Thus it affords the opportunity to lower intraocular pressure with doses that produce less renal and systemic effects of carbonic anhydrase inhibitors. At the lower dose levels in both man and rabbits, methazolamide induces essentially the same tonographic and aqueous humor chemistry changes as follow acetazolamide and other carbonic anhydrase inhibitors, but with less reduction of plasma bicarbonate and less systemic acidosis.[2] Methazolamide is also reported to have three to four times the anticonvulsant activity of acetazolamide in mice, but essentially the same diuretic activity.[3,4]

The present study compares methazolamide and acetazolamide as to their effectiveness in lowering intraocular pressure for short-term administration as well as for the long-term (over two years) therapy of glaucoma.

Method

Patients included in this series were selected from the Eye Clinic of the Department of Ophthalmology, Washington University School of Medicine, and from private patients referred to the department by members of its visiting staff. All patients included in the study had glaucoma that was uncontrolled (intraocular pressure 30 mm.

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Hg or higher) on miotic therapy.

Short-term methazolamide therapy was attempted in 89 patients (169 glaucomatous eyes). Seventy of the patients who responded well initially to such therapy were subjected to long-term methazolamide therapy for periods of over two years. Fifty of these 70 patients had failed previously to tolerate or to be controlled by acetazolamide. A series of 70 glaucoma patients treated for periods of over two years with acetazolamide were available for comparison.

Methazolamide* was administered in initial doses of 100 to 200 mg. every six to eight hours, followed by 150 to 450 mg. daily in divided doses; acetazolamide was administered in initial parenteral or oral doses of 250 to 500 mg. every four to six hours, followed by divided oral doses to a total of 500 to 2,000 mg. a day. Miotic therapy was continued in all patients.

Results

A. Short-term

Tonographic data on 169 eyes of 89 patients following short-term methazolamide are presented in Table 1 and compared with the results of a much larger acetazolamide series. Methazolamide suppressed aqueous secretion by more than 40 percent in 103 (61 percent) of the 169 eyes. Only 16 eyes (nine percent) failed to respond. When these figures are compared with the results of short-term acetazolamide therapy, it is apparent that the greater degrees of suppression of aqueous humor did not occur as frequently with methazolamide (61 percent of eyes) as with acetazolamide (83 percent of eyes). It should be noted, however, that a number of patients in the acetazolamide series who had acute glaucoma were treated with intravenous preparations, whereas all methazolamide was used orally.

B. Long-term methazolamide

The criteria for success utilized in this study were:

1. Intraocular pressure must have been maintained below 30 mm. Hg in both eyes at *all measurements*. Although this is a higher pressure level than ideal, in the patients with advanced uncontrolled glaucoma selected for this series, this pressure was considered adequate to avoid surgery, provided that there was no progression of field loss. Those patients whose eyes could be maintained at 24 mm. Hg or less are tabulated separately and were considered controlled in more satisfactory fashion.
2. No progression of loss of visual field occurred in either eye.
3. Side-effects did not prove intolerable.
4. Therapy was continued for a minimum of two years with adequate follow-up.

Patients who failed to meet any one of these criteria were classified as failures.

* Methazolamide and acetazolamide used in this study was provided by Lederle Laboratories, American Cyanamid Company, Pearl River, New York.

TABLE 1

Results of short-term methazolamide therapy in glaucoma

(169 eyes of 89 patients)

Glaucoma Diagnosis	No. of Eyes	Degree of Suppression of Aqueous Secretion		
		Over 40%	20–40%	0–20%
Chronic simple	122	72 (59%)	40 (33%)	10 (8%)
Secondary	22	16 (73%)	4 (18%)	2 (9%)
Angle-closure	25	15 (60%)	6 (24%)	4 (16%)
Total	169	103 (61%)	50 (30%)	16 (9%)
	Acetazolamide short-term results			
Total	440	366 (83%)	47 (11%)	27 (6%)

TABLE 2

COMPARISON OF LONG-TERM METHAZOLAMIDE AND ACETAZOLAMIDE THERAPY IN PATIENTS UNCONTROLLED BY MIOTICS ALONE

Glaucoma Diagnosis	No. Patients	Success*	
		$P_0 < 30$	$P_0 \leq 24$
METHAZOLAMIDE			
Chronic simple	56	18 (32%)	13 (23%)
Chronic secondary	8	2 (25%)	1 (13%)
Chronic angle-closure	6	2 (33%)	1 (17%)
TOTAL	70	22 (31%)	15 (21%)
ACETAZOLAMIDE			
Chronic simple	50	26 (52%)	21 (42%)
Chronic secondary	10	4 (40%)	1 (10%)
Chronic angle-closure	10	2 (20%)	0 (0%)
TOTAL	70	32 (46%)	22 (31%)

* In addition to above pressure criteria *in both eyes*, success is defined as no progression of visual field loss, tolerable side-effects, and a follow-up of over two years.

Table 2 compares the two-year follow-ups of 70 patients treated with methazolamide and 70 patients treated with acetazolamide, using the above criteria for evaluation of control. Acetazolamide appears to have been somewhat more effective than methazolamide in maintaining control of glaucomatous eyes, particularly in patients with chronic simple glaucoma. It is only fair to point out, however, that a large proportion of patients (50 of the 70) selected for methazolamide therapy had failed either to be controlled or to tolerate acetazolamide. Of the 20 patients not previously subjected to acetazolamide, methazolamide maintained intraocular pressure below 30 mm. Hg in eight (40 percent) and at 24 mm. Hg or less in five (25 percent). These latter percentages differ less from the acetazolamide data (46 percent below 30 mm. Hg and 31 percent at 24 mm. Hg or less).

It is of interest to compare the incidence of intolerable side-effects as a cause of failure of drug therapy. Such a comparison is made in Table 3. From Tables 2 and 3 it is apparent that if one chooses a pressure level of less than 30 mm. Hg as satisfactory control, about two thirds of the acetazolamide failures were on the basis of side-effects, whereas only about one third of the methazolamide failures were attributed to this cause. Similarly, at the 24 mm. Hg or less level, one half of the acetazolamide failures resulted from side-effects, but approximately 30 percent of the methazolamide failures were on this basis.

The side-effects necessitating discontinuing the administration of carbonic anhydrase inhibitors were somewhat different in the methazolamide and acetazolamide series (table 4). Although most acetazolamide failures were related to gastrointestinal (loss of appetite) or urinary (ureteral colic) symptomatology, methazolamide patients complained more of generalized malaise and excessive fatigue. These differences may be related to the greater penetration of methazolamide into the cerebrospinal fluid. Only one episode of ureteral colic occurred in the methazolamide series and this was in a pa-

TABLE 3

INCIDENCE OF INTOLERABLE SIDE-EFFECTS IN ATTEMPTED LONG-TERM METHAZOLAMIDE AND ACETAZOLAMIDE THERAPY

Carbonic Anhydrase Inhibitor	No. Patients	No. Discontinued Therapy Because of Side-Effects
Methazolamide	70	17 (24%)
Acetazolamide	70	24 (34%)

TABLE 4

INCIDENCE OF PRINCIPAL SIDE-EFFECT NECESSITATING DISCONTINUING LONG-TERM CARBONIC ANHYDRASE INHIBITION

	Methazolamide (70 patients)	Acetazolamide (70 patients)
Gastrointestinal	4	14
Generalized malaise	7	0
Excessive fatigue and drowsiness	4	0
Urinary	1	8
Hearing loss	0	1
Leukopenia	1	0
Skin rash	0	1
TOTAL	17	24

tient who had experienced several such attacks on acetazolamide (and similar episodes before carbonic anhydrase inhibitors were used). No ocular toxicity was noted in either the acetazolamide or methazolamide treated patients.

In the course of these studies methazolamide therapy was attempted in 50 patients who were classified as failures on acetazolamide, 16 on the basis of poor control and 34 who could not tolerate the side-effects of the drug. The results in this series of patients are presented in Table 5. It is apparent that the effectiveness of methazolamide therapy in the 50 acetazolamide failures was quite similar to the total methazolamide series of 70 patients. More significantly, some two thirds of patients who could not tolerate the side-effects of acetazolamide were able to tolerate methazolamide and half of these could be maintained under satisfactory control. Very few patients (two out of 16) could be controlled on methazolamide when the cause of acetazolamide failure was poor control.

COMMENT

SHORT-TERM METHAZOLAMIDE

It is clear from the results in this series that methazolamide is an effective agent for short-term administration in the acute and chronic glaucomas. Unfortunately no intravenous preparation of methazolamide is available. This may account for its being not quite as effective as acetazolamide. It has become our practice to restrict the use of methazolamide to those few patients who fail to respond or who cannot tolerate short-term acetazolamide therapy.

LONG-TERM THERAPY

A significant number of patients with chronic glaucoma not controlled by miotics can be brought under more satisfactory control by the addition of acetazolamide or methazolamide to their therapeutic regimen. Although in the present study acetazolamide produced a somewhat higher success rate than methazolamide, it is important to re-emphasize that the methazolamide series of 70 patients contained 50 acetazolamide failures. It is also important to point out that the cause of failure in acetazolamide therapy was predominantly intolerable side-effects, whereas with methazolamide therapy, poor control was a major limiting factor.

From the practical point of view the important fact emerges that many patients who

TABLE 5

ATTEMPTED LONG-TERM METHAZOLAMIDE IN ACETAZOLAMIDE FAILURES (50 PATIENTS)

Cause of Acetazolamide Failure	No. Patients	Methazolamide Success*		Intolerable Side-Effects
		$P_0 < 30$	$P_0 \leq 24$	
Control ($P_0 \geq 30$)	16	2 (13%)	2 (13%)	1 (6%)
Side-effects	34	12 (35%)	8 (24%)	12 (35%)
TOTAL	50	14 (28%)	10 (20%)	13 (26%)

* In addition to above pressure criteria *in both eyes*, success is defined as no progression of visual field loss, tolerable side effects, and a follow-up of over two years.

il to tolerate acetazolamide can be con-olled successfully for periods of over two ars on methazolamide therapy. With both rugs available in addition to miotics and e administration of methazolamide to the etazolamide failures, it becomes possible maintain pressure levels below 30 mm. g in approximately 60 percent of patients ith chronic glaucoma uncontrolled on mi-ics; and over 45 percent of patients with herwise uncontrolled glaucoma can be im-roved to pressure levels of 24 mm. Hg or ss at all measurements. In patients with reviously uncontrolled chronic simple glau-oma such use of both agents in addition to iotics proves even somewhat more promis-g. Thus approximately two thirds of pa-ents with chronic simple glaucoma uncon-olled on miotics can be regulated at pressure vels below 30 mm. Hg, and over 55 percent of these patients are kept at pressures of 24 mm. Hg or less at all measurements over a two-year period.

Summary

Methazolamide (Neptazane) is a carbonic anhydrase inhibitor which lowers intraocular pressure in much the same fashion as acetazolamide (Diamox). Although not quite as effective as acetazolamide in controlling intraocular pressure, methazolamide reduces aqueous formation at lower dose levels and induces fewer (and different) systemic side-effects. Methazolamide finds its major usefulness in the long-term therapy of patients with uncontrolled chronic glaucoma who fail to tolerate other carbonic anhydrase inhibitors.

640 South Kingshighway (10).

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THE TREATMENT OF EALES' DISEASE BY ROENTGEN THERAPY*

Algernon B. Reese, M.D., and Ira S. Jones, M.D.
New York

Introduction

The multiplicity of reports in the literature mentioning various methods of treatment of diseases of the retina characterized by new-formed blood vessels is sufficient indication that no satisfactory treatment has yet appeared. More and more it becomes apparent that so-called Eales' disease represents a heterogeneous group of lesions. A vascular disease of the retina which can cause vitreous hemorrhage requires a rather thorough investigation now because of the increasing number of possible etiologic causes. This has become so impressed on us of late that we have listed the conditions which must be considered in etiologic work-up. This is as follows:

Blood dyscrasias	Arteritis and periarteritis
Anemias of various sorts	Phlebitis and periphlebitis
Clotting deficiency (PTA deficiency, Hemophilia)	Lupus erythematosis
	Collagen diseases in general

*From the Institute of Ophthalmology of the Presbyterian Hospital and the Department of Ophthalmology, Columbia University, College of Physicians and Surgeons.

Sickle-cell disease	Vascular disease + deposits
Macroglobulinemia	Idiopathic vascular disease (Coats, v. Hippels, Eales)
Cryoglobulinemia	Pheochromocytoma
Diabetes	
Polycythemia rubra vera	

In the past roentgen therapy has been advocated[1,2] but this modality was given at the time when Eales' disease was viewed more as an entity than it is now. Because of the different entities which are included under the heading of Eales' disease it is not surprising that some have reported successes, others failures and in general the results have been unpredictable and unsatisfactory.

We would like to report two cases of so-called Eales' disease which have been successfully treated by X-rays. This estimate of the treatment is based on the fact that the eye treated has not shown a steadily progressive course and the fellow eye which is untreated has come to enucleation. It might be argued that some cases in this group do take a course even without treatment where there is a disparity in the progress in the two eyes. The assumption, however, here seems to be logical that X-ray therapy has been an important factor in salvaging one of the eyes. The report of these two cases is as follows:

Presentation of cases

Patient D. B.

Beginning in 1945 at about the age of 25 years, this patient had a retinal vascular disease characterized by tufts of new-formed capillaries with grapelike clusters of aneurysmal dilatations associated with them. These could be observed from both the arterial and the venous side. The left eye was more heavily involved than the right and showed a detachment of the retina below. There was also fibrous tissue and new-formed blood vessels extending into the vitreous from the area of the disc. The patient's course was characterized by recurrent hemorrhages into the vitreous followed by clearing.

In 1948, the vision of the right eye was 20/50 and of the left 20/70.

In March, 1948, radiation was started. The factors were as follows: 220 kv., 20 ma., 50 cm. target skin distance, 0.5 mm. copper plus 1.0 mm. aluminum filter, 2.5 cm. portals, 500 per treatment for a total of 2500 r × 2, right temple 2500 r, left temple 2500 r. This treatment was given over a three-week period.

During the year subsequent to this radiation the patient felt that the vision declined progressively in his right eye and he felt that his left eye was useless. However, when seen in July, 1949, the vision in the right eye was found to be 20/15 and in the left 20/40.

The right fundus exhibited coiled tortuous dilated vessels below the disc and hemorrhage above the disc. No detachment was present. The left exhibited a massive retinitis proliferans with detachment below. No further irradiation was done at this time.

The patient was not seen again until 1953 but in the interim had two hemorrhages in the right eye at intervals of two years and three years after completion of irradiation. The vision was found to be 20/15 in the right and 20/200 in the left eye. A fundus drawing of each eye was made at this time and the right is shown in Figure 1. During the subsequent year the patient had a few hemorrhages in the right eye which cleared. A drawing made in March, 1945, of the right fundus is shown in Figure 2. A new drawing of the right fundus was made in December, 1954, and is shown in Figure 3. In April, 1955, the patient was seen and it was definite that the right fundus showed less abnormal change than previously. The left eye developed secondary glaucoma and a cataract and in March, 1956, was removed. The last drawing on this patient was made in February, 1958, at which time the vision in the right eye was 20/20 (fig. 4).

Patient Y. Z.

This patient had a history of healed pulmonary tuberculosis. Beginning in 1945 at about the age of 20 years, vitreous hemorrhages appeared first in the left eye and then in the right. Following these vitreous hemorrhages retinitis proliferans developed. Evidence of periphlebitis could be detected in the areas from which the retinitis proliferans extended.

Fig. 1 (Reese and Jones). *Patient D. B.* Fundus drawing made eight years after onset of retinal vascular disease and five years after irradiation treatment. The fundus disease was thought to be slightly more pronounced over the status at the start of irradiation.

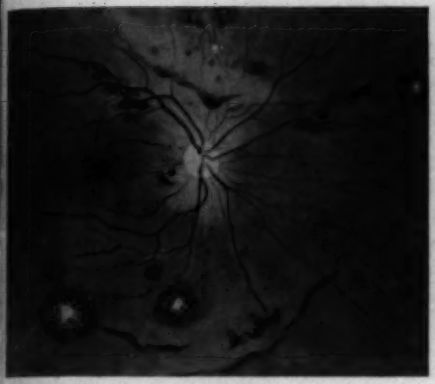

Fig. 2 (Reese and Jones). *Patient D. B.* Fundus drawing six years after irradiation with apparent advancement in the retinal vascular disease.

The retina in the left eye became detached about two years later, and surgery to attempt reattachment was carried out. This was not successful. Vitreous hemorrhages continued in both eyes and, in 1948, the vision in the right was 20/15 with the best correction and in the left counting fingers at four feet. The right fundus showed hemorrhages adjacent to the disc nasally and extending into the vitreous. There was also translucent tissue with blood vessels extending into the vitreous from the region of the disc. The left fundus showed a detached retina but details were poorly seen.

Medical treatment with antihemorrhage measures was carried out but was without avail. In August, 1949, the situation showed some progression in the right eye and a drawing was made at that time (fig. 5).

X-ray treatment was begun. The factors were 220 kv., 20 ma., 50 cm. target skin distance, 0.5, mm. copper + 1.0 mm. aluminum filter, 2.5 cm. portal, 250 per treatment for 12 treatments with a total of 3,000 r directed to the right temple.

Fig. 3 (Reese and Jones). *Patient D. B.* Fundus drawing seven years after irradiation, showing regression of the retinal vascular disease.

Fig. 4 (Reese and Jones). *Patient D. B.* Fundus drawing 10 years after radiation, showing regression and apparent arrest of the retinal vascular disease.

When seen about one year later it was still not possible to tell whether any regression had taken place. Three years after the treatment the vision in the right eye remained 20/15 and it was felt there had been no progression. Definite decrease in the picture, however, was not yet apparent. The patient was seen again in January, 1957, almost eight years after roentgen therapy and the right eye was quiet. Definite regression of the retinitis proliferans, aneurysmal dilatations and hemorrhages had taken place (fig. 6).

Discussion

Unfortunately the second case presented here was not observed at sufficiently short intervals to determine the course following

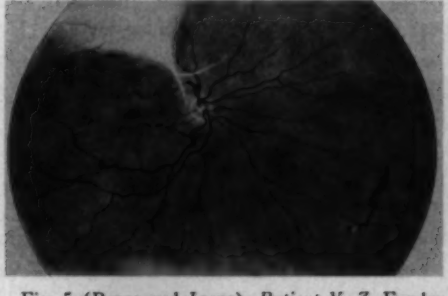

Fig. 5 (Reese and Jones). *Patient Y. Z.* Fundus drawing approximately four years after onset of retinal vascular disease. Radiation treatment had been given one month earlier.

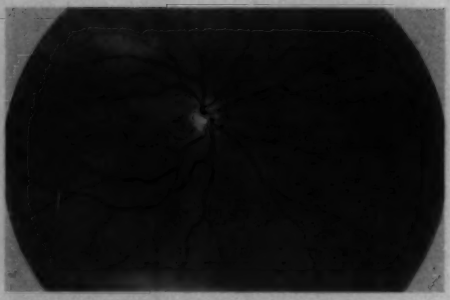

Fig. 6 (Reese and Jones). *Patient Y. Z.* Fundus drawing of the same eye eight years after X-ray treatment, showing essentially no pathologic change.

radiation treatment. The first patient, however, showed continued progression of retinal vascular disease following radiation. Whether this was the natural history of his disease, or whether the changes were aggravated by radiation is not apparent. He then showed a slow but, to the present time, steady improvement and regression in the retinal vascular disease. It may be that eyes only moderately affected may tolerate the period of progression which may follow radiation therapy and when enough time has passed may then show the beneficial effects of the therapy. In any event, the two cases showed herewith are sufficiently favorable to indicate the desirability of further studies on the effect of irradiation in retinal vascular disease.

It is worthy of note that the untreated eye in each case was lost.

Our opinion at the present time may be best expressed by the following quotation:

> I feel that the appraisal of the late results in the treatment of Eales' disease by roentgen therapy by Anjou and Cederquist is well executed and fair. Certainly such a follow-up report on the treatment of these cases is long overdue. Factors contributing to this delay are the rarity of the condition and the difficulty in determining whether the treatment has altered the course of the disease. A great deal of time must elapse between the time of treatment and the time when an ultimate result can be judged. Furthermore, I am not sure that we do not include more than one entity in our diagnosis of Eales' disease. It seems probable that several conditions characterized by vitreous hemorrhage are included under this term. If so, another difficulty is added to the evaluation of the treatment.
>
> Certainly we have a few instances of so-called Eales' disease characterized by the rete mirable in which one eye has been blinded from the disease and X rays have been given to the fellow eye resulting over a long period of years in a more or less nonprogressive course. However, the cases are few, and this may be a manifestation of the natural course of the disease. In the majority of the cases the disease has shown a relentless progression.
>
> In general, I would say that there can be no doubt that X rays may cause a regression of the neovascularization or rete mirabile, but that X rays probably have no beneficial effect on the ultimate course of the disease. There are nevertheless a few cases which seem to belie this assessment and for this reason I do not feel free to condemn the treatment without reservation.
>
> I feel confident that in cases of diabetic retinopathy, which are characterized by neovascularization, X ray has absolutely no beneficial effect, and occasionally the clinical impression is that it may have hastened some retinal vascular insults.
>
> Algernon B. Reese.[2]

These two cases suggest that in heterogeneous group of so-called Eales' disease there is one type of case that may be benefited by radiation. We hope that the report of these two apparently successfully treated cases will help to identify the types which may respond to this modality. In the end we may be able to ferret out of this group the ones in which X-ray therapy can be advocated.

Summary

Two cases of retinal vascular disease treated by irradiation are shown 10 and eight years after the treatment with favorable results.

73 East 71st Street (21).

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THE CORRECTIVE TREATMENT OF AMBLYOPIA WITH ECCENTRIC FIXATION*

HEINZ GÖRTZ, M.D.
Düsseldorf, Germany

Despite the effectiveness of combined orthoptic and surgical treatment in strabismus, in many instances amblyopia presents itself as a barrier to binocular vision. It is for this reason that more adequate means of diagnosis and treatment of amblyopia must be considered. The purpose of this paper is to evaluate a new form of treatment of amblyopes with eccentric fixation.

Occlusion therapy has proved to be effective in some but not all amblyopes with foveal fixation. In patients with eccentric fixation occlusion therapy of the nonamblyopic eye is contraindicated. The therapeutic procedures for patients with eccentric fixation will be outlined.

The improvement of the visual acuity is not the only aim. The first attempt in the management of eccentric fixators is to achieve foveal fixation and proper localization to the central mechanism. Subsequent bifoveal stimulation may then produce normal binocular function. Optimum visual acuity may now be achieved since the prerequisite of centralization of fixation has been established. Finally, only normalized binocularity will serve as a barrier against relapses of the so-called cured amblyopes.

This paper will present a critical analysis of 88 amblyopes with eccentric fixation treated in accordance with the principles already mentioned. The patients were hospitalized for the duration of therapy. They do not represent a favorable group since they had all been treated previously without success. This group consists of individuals between six and 22 years of age with an average age of 9.7 years.

Although conventional occlusion therapy is not utilized in cases of eccentric amblyopia, primary occlusion of the central fixing (normal) eye in children is still performed up to the age of four years. It is well known that a spontaneous shift of fixation is only exceptionally possible after the age of five years and the danger of strengthening the eccentric fixation by occluding the good eye increases with age. Persistent eccentric fixation would not only prevent optimum visual acuity but, above all, would prevent normal binocularity.

METHOD

All patients were retinoscoped after proper atropinization. The corrections were given as found on retinoscopy half a diopter of sphere subtracted to insure better tolerance of the prescription. All visual acuities were checked with numbers.

After glasses had been worn for a minimum period of three months, treatment began with occlusion of the eccentrically fixing amblyopic eye. For the active change of fixation and localization, we utilized the after-image method of Cüppers.[1] To position the amblyopic eye properly a small mirror was used in front of the nonamblyopic eye, permitting the patient to fix a small object and then guide him into the desired position by turning the mirror. Utilizing the Euthyscope with a light of medium intensity, the posterior pole of the retina is then stimulated in a circle of 30 degrees of arc. The fovea centralis is spared by the presence of a centrally located disc shielding an area of three to five degrees of arc. The stimulation should not be applied for more than 30 seconds.

After the application of the Euthyscope the patients should see at first a disclike positive after-image with a black spot in the center. Frequently there is a spontaneous change into a negative after-image. The central "spared-zone" will then appear as a clear greenish disc. Since this disc corresponds to

* From the Eye Clinic of the Academy of Medicine (Director: Prof. Dr. med. E. Custodis).

the macular area, the patient will in this manner be made aware of the desired foveal projection. By repeated changes of the after-images, this impression will be intensified. The after-image variation is enhanced by rapidly changing the room's total illumination between darkness and brightness. The change of after-images can also be provoked by closing the eyes.

In order to acquaint the patient with the positive and negative after-image we utilize first the nonamblyopic eye, since it is very easy in almost all patients to elicit this phenomenon. In contradistinction the amblyopic eye with eccentric fixation does not appreciate a positive or negative after-image spontaneously, and this is at times a very laborious process to teach the recognition of positive and negative after-images. The ease with which patients can be made aware of the after-image change is of marked prognostic value.

Once the patients have been taught to appreciate a positive or negative after-image they are ready for further instruction. They are told to place their negative after-image in such a way that they cover with it a red disc (15-cm. diameter) fixed on a white screen six meters away. In the beginning this seems to be difficult due to inaccurate localization of the after-image in space. (In eccentrically fixating amblyopes, the fovea does not give a "straight ahead" impression.) Step by step the patients learn to associate the impression of "straight ahead" with the regained central fixation. It is an adaptation of the new foveal awareness to extraocular muscle innervation and to proprioceptive impulses.

After centralization of fixation there is seen a corresponding improvement of the visual acuity for isolated letters. It is not advisable to stimulate the central retinal function too early with a single letter (optotype). Should the patient utilize parafoveal areas within the central after-image, there exists the possibility of creating new pseudofoveolas if central fixation is not well established. This point will be important in the discussion of "separation difficulties," a criterion of all amblyopes. (It is well known that a visual acuity taken with a single letter will frequently be much higher than when taken on a row of letters. This condition is called "separation difficulties" [Bangerter[2]].)

When the patients are able to fix centrally within an area of two degrees of arc, the Koordinator of Cüppers is used for further improvement of fixation and localization. The principle employed by this instrument is the Haidinger brush phenomenon. Because of the anatomic structure of the retina, the polarized lightbeam will cause the known spindle-shaped effect in the foveal area only. The rotation of the polarization prism prevents local adaptation. If the patients are able to see the rotating spindle (the "propeller"), central fixation is adequate. Later, co-ordination of the proper localization between eye and hand is trained by copying stencils superimposed upon the rotating prism.

The co-ordination of monocular localization with other sensory receptors is of the utmost importance and this ability is further developed by utilizing the Korrektor of Bangerter.[2] Should the patient, because of faulty monocular localization, fail properly to follow the lines of a stencil, a red lamp flashes and a buzzer sounds. Thus, hearing and peripheral retinal impulses can be coordinated with foveal localization and proprioceptive impulses of the eye muscles, the hand, and the neck position reflexes.

The "Separation-trainer" of Bangerter[2] is used to stimulate the ability to separate and recognize forms. The fovea is stimulated with optotypes (single E-signs) which can be separated from each other at varying distances. Also, the distance of the patient from the apparatus may be altered. The Korrektor and Separation-trainer should be used only after central fixation has become secure. Otherwise more harm than good will result. Fixation must be controlled during the exercises with the Visuscope star. (With the

Visuscope, a special ophthalmoscope, a star can be projected onto the fundus and the patient has to fix the star. The ophthalmologist then can analyze exactly the point of fixation of the retina.) If central fixation is not constant, one must again resort to the use of after-images (Euthyscope).

Results with the described Separation-trainer are not as good in formerly eccentrically fixating patients as they are in those with primary central fixation. This can probably best be explained by the rivalry between the eccentric pseudofovea and the fovea centralis and the multiple, possible transitory pseudofoveas. Intelligent patients frequently describe spontaneously the anticipated phenomenon of monocular diplopia and triplopia.

When central fixation (normal spatial projection of the fovea) is established, the better eye is then occluded. In the presence of marked muscle imbalance, surgery is performed prior to functional training. Smaller angles of squint are operated upon during the training period.

Intensive binocular therapy is started as soon as fixation proves to be adequate. Exercises are performed with the Synoptophor and in "free space" with a polarization projector. (Polarized light allows the compensation of the angle of squint in free space.) In cases of inconsistent central fixation binocularity can be trained by producing the Haidinger brush phenomenon in one arm of the Synoptophor (on the side of the amblyopic eye). A special construction of the Cüppers Synoptophor enable us to do this.

In cases of extreme fixation nystagmus the use of the Euthyscope can be difficult. As soon as centralization lies within two degrees of arc the co-ordinator may be of more and special value.

Results and Discussion

Table 1 shows the results of monocular and binocular training. The eccentric fixators are separated into parafoveolar, paramacular and far eccentric fixations. Furthermore the term "no fixation" is used. As to binocular function we distinguish normal (NC) and anomalous retinal correspondence (AC). The degree of binocularity is measured in comparison to the obtained stereopsis. Degree 0-1 denotes insufficient, degree 2 medium and degree 3 maximum stereopsis. (Stereopsis is measured on the Synoptophor and with polarized light in "free space.")

Of the 88 patients with eccentric amblyopia treated, 71 or 80.7 percent developed central fixation; 17 or 19.3 percent were resistant to therapy. Among the patients with centralized fixation, we distinguish between quiet central, restless central, and marked nystagmoid fixation—53.4 percent manifested quiet central fixation, 18.2 percent restless central fixation, and 9.1 percent marked fixation nystagmus. The failures were composed of two groups—absolute (11.4 percent) and relative failures (7.9 percent), the latter exhibiting temporary changes of fixation (table 2).

The visual acuity ultimately obtained may be expressed by establishing three groups: Acuities from 0.7 to 1.0, from 0.4 to 0.6 and those of less than 0.4. Of the amblyopes with eccentric fixation treated 35.3 percent were in the optimal group, 32.9 percent belonged to the middle group and 31.8 percent achieved a visual acuity of less than 0.4 (table 3).

Of special importance is the analysis of the binocular function of the 71 patients who exhibited a change of fixation. As expected, 88.7 percent originally had anomalous correspondence. We succeeded in getting a change of correspondence in 77.4 percent of the patients. In evaluating the final retinal correspondence acquired with regards to stereopsis, the following distribution was noted: 22.5 percent of the patients with centralization of fixation obtained high quality stereopsis after intensive binocular training; 29.6 percent acquired partial stereopsis, whereas 25.3 percent fulfilled only several of the criteria of normal correspondence. (table 4). Of the patients with centralization of

TABLE 1

RESULTS OF MONOCULAR AND BINOCULAR TRAINING IN 88 CASES OF ECCENTRIC AMBLYOPIA

Case	Age (yr.)	Fixation		Visual Acuity		Binocularity		Sessions	
		Before	After	Before	After	Primary	Secondary	Monocular	Total
1	9	p-mac	C	0.15	0.7	AC	NC3	11	21
2	10	p-fov	C	0.3	0.7	AC	NC3	9	33
3	14	p-fov	C	0.05	0.4	NC	NC3	5	27
4	7	f-exc	±C (Nys)	0.05	0.3	AC	NC1	21	34
5	15	p-mac	C	0.2	1.0	AC	NC3	12	26
6	7	p-mac	C	0.1	0.9	AC	NC2	12	29
7	9	f-exc	±C (Nys)	0.05	0.4	AC	NC1	14	27
8	5	p-mac	C	0.15	0.7	AC	NC1	14	36
9	16	p-mac	p-mac	0.1	0.15	—	—	15	15
10	10	p-mac	C	0.2	0.7	AC	NC3	20	44
11	7	p-fov	C	0.1	0.4	AC	NC0–1	9	24
12	10	p-mac	C	0.2	1.0	AC	NC3	19	63
13	11	p-fov	C	0.25	0.7	NC	NC3	8	16
14	6	p-fov	C	0.15	0.7	AC	NC3	9	16
15	11	f-exc	±C	0.05	0.3	AC	AC	17	21
16	9	n-fix	±C	0.05	0.15	AC	NC1	16	30
17	7	p-fov	C	0.15	0.7	AC	NC2	13	26
18	13	n-fix	±C	0.05	0.15	AC	NC0–1	9	23
19	7	p-mac	±C	0.1p	0.4	NC	NC2	16	27
20	8	p-fov	C	0.1	0.4	AC	NC1	4	35
21	15	p-mac	C	0.1p	1.0	AC	NC3	18	35
22	6	p-mac	±C	0.2	0.5	AC	AC	12	17
23	7	p-fov	C	0.1	0.7	AC	NC2	16	29
24	13	p-fov	C	0.2	0.5	NC	NC3	9	15
25	13	p-mac	C	0.15	0.7	AC	NC1	15	28
26	8	p-fov	C	0.3	0.7	AC	NC3	13	27
27	13	p-fov	C	0.3	0.7	AC	NC2	10	29
28	7	f-exc	±p-mac	0.05	0.1	—	—	28	28
29	14	p-mac	±C	0.05	0.4	AC	AC	26	45
30	13	p-mac	C	0.05	0.7	NC	NC2	15	24
31	10	p-fov	C	0.3	0.7	AC	NC2	3	15
32	11	p-fov	C	0.3	1.0	AC	NC2	2	25
33	8	f-exc	p-fov±C	0.05	0.15	AC	AC	24	27
34	10	p-mac	C	0.25	1.0	AC	NC3	12	20
35	7	p-fov	±C	0.1	0.4	NC	NC2	7	17
36	7	p-mac	C	0.1	1.0	AC	NC3	20	61
37	9	p-mac	C	0.05	0.5	AC	AC	23	39
38	11	p-mac	±C	0.2	0.5	AC	NC3	12	28
39	8	p-mac	C	0.1	1.0	AC	NC2	24	50
40	8	f-exc	±C	0.1	0.4	AC	NC0–1	17	35
41	22	p-mac	C	0.1p	0.4	AC	NC0–1	8	10
42	9	p-fov	C	0.15	0.7	NC	NC0–1	5	11
43	10	p-mac	C	0.1p	0.5	AC	NC2	5	31
44	7	n-fix	n-fix	0.05	0.1	—	—	15	15
45	8	p-mac	p-fov±C	0.2	0.5	—	—	14	14
46	7	p-mac	C	0.1	0.4	AC	NC2	12	36
47	8	p-mac	±C (Nys)	0.15	0.4	AC	AC	44	52
48	8	f-exc	±C	0.05	0.2	—	—	20	30
49	8	f-exc	C	0.2p	0.7	AC	AC	10	35
50	8	p-mac	C	0.05	0.2	AC	NC0	18	32
51	11	p-fov	C	0.25	0.5	AC	NC2	20	34
52	14	p-mac	C	0.05	0.5	AC	NC0–1	13	16
53	7	f-exc	±p-mac	0.02	0.1	—	—	12	12
54	6	p-mac	p-fov (Nys)	0.05	0.05	—	—	26	26
55	6	p-fov	C	0.1	0.5	AC	NC0	20	28
56	13	p-mac (Nys)	±C (Nys)	0.05	0.3	—	—	20	22
57	7	p-mac	C	0.15	0.7	AC	NC2	10	32
58	8	n-fix	p-fov±C	0.05	0.35	—	—	25	26
59	7	p-fov	C	0.15	0.4	AC	NC0	14	28
60	9	f-exc	±C	0.2	0.35	AC	AC	30	36
61	8	p-fov	C	0.25	0.7	AC	NC2	12	32
62	7	p-fov	C	0.25	1.0	AC	NC2	8	38
63	8	f-exc	±C (Nys)	0.05	0.2	AC	AC	28	30
64	12	f-exc	±C	0.1	1.0	AC	AC	25	42
65	9	f-exc	p-mac	0.02	0.2	—	—	24	24

TABLE 1 (*Continued*)

Case	Age (yr.)	Fixation		Visual Acuity		Binocularity		Sessions	
		Before	After	Before	After	Primary	Secondary	Monocular	Total
66	15	f-exc	p-fov ±C	0.05	0.1	—	—	26	26
67	10	p-mac	C	0.15	0.5	AC	AC	43	62
68	9	f-exc	±C (Nys)	0.05	0.35	AC	NC2	45	56
69	10	p-mac	C	0.05	0.4	AC	NC2	49	68
70	13	f-exc	p-fov ±C	0.05	0.15	—	—	26	28
71	7	p-mac	C	0.3	1.0	NC	NC2	2	12
72	13	p-fov	±C (Nys)	0.3	0.4	AC	AC	10	20
73	11	n-fix	p-mac	0.05	0.2	—	—	28	30
74	9	p-mac	C	0.1	0.3	AC	NC0	16	32
75	9	p-mac	C	0.05	0.5	AC	NC2	36	56
76	7	n-fix	±C	0.02	0.3	AC	AC	28	30
77	14	f-exc	p-fov	0.05	0.4	—	—	30	30
78	13	p-mac	±C	0.1	0.3	AC	NC3	6	20
79	8	n-fix	C (Nys)	0.05	0.5	AC	AC	11	20
80	10	p-mac	C	0.1p	0.7	AC	NC0–1	8	48
81	10	f-exc	±C	0.05	0.4	AC	AC	35	46
82	7	p-mac	p-mac ±C	0.02	0.15	—	—	32	32
83	9	p-fov	C	0.2	0.7	AC	NC3	6	28
84	9	f-exc	p-fov ±C	0.05	0.3	AC	AC	58	73
85	10	p-mac	C	0.15	0.4	AC	NC2	8	24
86	17	p-fov	C	0.3	1.0	AC	NC2	18	26
87	7	n-fix (Nys)	n-fix (Nys)	0.03	0.1	—	—	6	6
88	9	p-mac (Nys)	p-mac (Nys)	0.1	0.15	—	—	14	14

C = central; p-fov = parafoveolar; p-mac = paramacular; f-exc = far-eccentric; n-fix = no fixation; Nys = nystagmus; NC = normal, AC = anomalous correspondence.

fixation, 52.1 percent obtained useful stereoscopic vision.

It is important to note that the 88 patients analyzed in this paper had an average of 17.5 sessions of monocular training and a total of 30.2 sessions of combined monocular and binocular training (one session = one-half hour). When possible, the patient should be hospitalized. Therapy is more effective when multiple five-minute sessions are utilized in preference to prolonged sessions at greater intervals.

The importance of adequate surgical correction during the functional treatment period must be emphasized. If the eyes are not parallel, the patient is unable to use the newly acquired normal function in "free space." Also the danger of regression to the former status is an ever-present possibility. Frequently cases which were resistant to therapy exhibit normal function followed surgery. In part, we are dealing here with the facts I have described as "the fractioned change of correspondence."[3]

While stressing the primary importance of fixation and localization, it is not my intention to minimize the subjective and objective value of the improvement of visual acuity. I am interested ultimately in accomplishing that visual acuity necessary for binocular function. In analogy to anisometropia the tolerable difference is limited. In my experience, however, marked differences in the visual acuity of both eyes still permit binocular function. As a rule I like to state that a visual acuity of 0.4 in the amblyopic eye makes binocular training feasible. Binocular success in those with visual acuities of less than 0.4 is the exception.

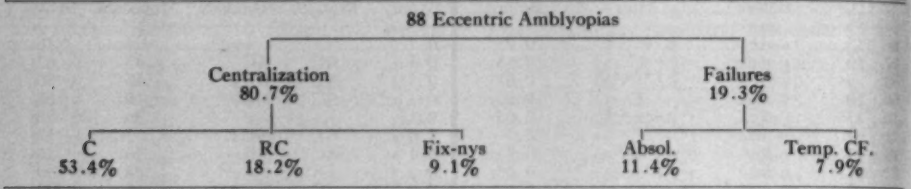
Investigations with polarized light have proved the existence of marked differences in the visual acuity of the amblyopic eye dependent upon monocular or binocular examination. There is a close connection between the different inhibition scotomas of monocular or binocular testing. Investigation of this matter is not yet finished.

After the conditions for binocular train-

TABLE 2

CHANGES OF FIXATION

(Expressed as percentage)



C = quietly central; RC = restless central; Fix-nys = fixation nystagmus; Temp. CF. = temporary change of fixation.

TABLE 3

FINAL VISUAL ACUITY

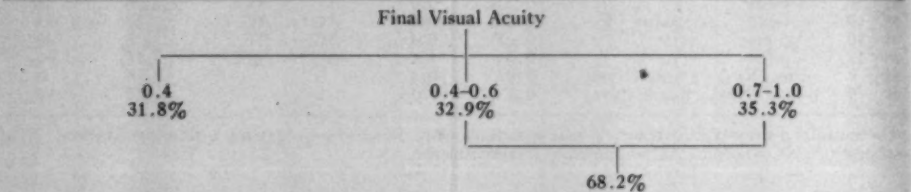
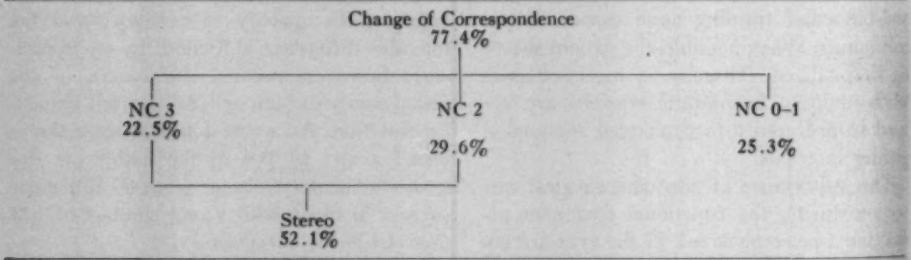


TABLE 4

NORMALIZATION OF CORRESPONDENCE

(Distribution according to stereopsis)



NC0–1 = insufficient stereopsis; NC2 = medium; NC3 = high quality stereopsis.

ing have been fulfilled the further improvement of visual acuity must be assiduously fostered.

In conclusion, amblyopia with eccentric fixation, like all amblyopias, cannot be regarded and treated as an isolated phenomenon. Without discussing the other etiologies of amblyopia, I am of the opinion that the amblyopia present in cases of strabismus is mainly an adaptation to the faulty alignment of the visual axes. Change of localization and inhibition scotomas are products of this adaptation. Without good binocular function in "free space," there must be a new pathologic adaptation to the new squint situation. Therefore, it is useless to expect

centralization of fixation, proper localization and the loss of the inhibition scotomas by improving visual acuity alone. These are all prerequisites of the corrective treatment, but not the final aim. Considering the whole therapeutic concept, it must be stated, that, with the newly established binocularity, a more nearly permanent cure of the formerly eccentrically fixating amblyope is achieved.

Summary

Basic aims of the corrective treatment of amblyopia with eccentric fixation should be in this sequence of importance: change of fixation, monocular localization, and the improvement of visual acuity. This paper reports 88 cases of amblyopia with eccentric fixation, the results of which are discussed with regard to fixation, monocular localization, visual acuity, and the degree of binocularity attained.

Eye Clinic, Academy of Medicine.

I wish to thank Miss Esther Widmer, orthoptist, for her technical assistance.

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THE EFFECT OF HYDROCHLOROTHIAZIDE (ESIDREX) ON INTRAOCULAR PRESSURE IN MAN*

Romeo V. Fajardo, M.D., Ralph Hamilton, M.D., and Irving H. Leopold, M.D.

Philadelphia, Pennsylvania

A new oral diuretic, hydrochlorothiazide (6-chloro-3, 4-dihydro-7-sulfamyl-2H-1, 2, 4-benzothiadiazine 1, 1-dioxide) (Esidrex†) has been found to be 10 to 20 times as potent as chlorothiazide. It is also an effective hypotensive drug. Being related to chlorothiazide it acts more closely as a mercurial diuretic rather than as a carbonic anhydrase inhibitor. It is a weak carbonic anhydrase inhibitor.[3, 4, 7–9] Nevertheless clinical studies had been done to evaluate its possible usefulness in lowering human intraocular pressure.

Materials

A total of 45 patients with 68 nonglaucomatous and 37 patients with 57 glaucomatous eyes were chosen from the ward cases of the Wills Eye Hospital. All these patients were hospitalized in order to observe closely the ocular and systemic effects relative to the administration of the drug.

Nonglaucomatous eyes in this study are those cases which have an intraocular pressure of 25 mm. Hg (Schiøtz) or lower with negative history of glaucoma and with absent optic disc cupping, normal tonographic patterns and, where indicated, negative provocative tests.

Glaucomatous eyes in this study are those that give history of rises in intraocular pressure above 25 mm. Hg (Schiøtz). All of them have ophthalmoscopic, perimetric, tonographic and gonioscopic studies to confirm the

* From the Wills Eye Hospital.

† This drug was investigated as Su-5879 and was supplied by Ciba Pharmaceutical Products, Inc., Summit, New Jersey.

diagnosis. They are composed of various types of glaucoma.

Another 14 patients with 21 nonglaucomatous eyes were chosen to serve as controls.

Methods of Study

The effect of a single oral dose of the drug on the intraocular pressure is the main theme of this study. Doses of 50, 100 and 150 mg. were tried in various groups of patients and were given at 9:00 A.M. Hourly tonometric readings were taken by the same individual using the same Schiøtz tonometer from 9:00 A.M. to 3:00 P.M. Pontocaine hydrochloride (0.5 percent) was used as topical anesthetic.

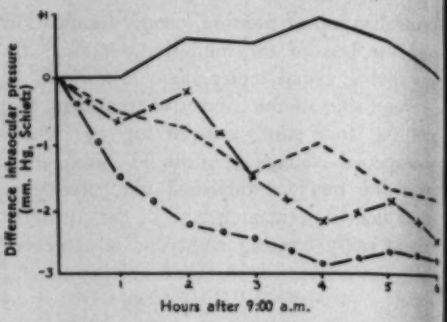
All hypotensive and diuretic drugs were discontinued the night previous to the test.

Antiglaucoma drugs, systemic or local, were stopped the night previous to the test in all the glaucoma cases. If the intraocular pressure had been lowered or controlled by antiglaucoma therapy before the test only those cases in which tensions were 25 mm. Hg (Schiøtz) or more at the time of the initial reading were included in this series.

The 14 patients with 21 nonglaucomatous eyes who serve as controls received no medications and had tonometric readings from 9:00 A.M. to 3:00 P.M. This was done to compare the possible diurnal variations of the intraocular pressure during the period of study.

Results of the Study

The results of this study were summarized as averaged differences of intraocular pressures in mm. Hg (Schiøtz) subsequent to the administration of the drug compared to the initial reading, that is, the tonometric reading before the ingestion of the drug.



Graph 1 (Fajardo, Hamilton and Leopold). Hourly changes in intraocular pressure of nonglaucomatous eyes (average) from 9:00 A.M. to 3:00 P.M. (——— no medicine, - - - -, 50 mg., o-o-o-o-100 mg., x-x-x-x-, 150 mg.)

The hourly average variations in the intraocular pressure of the control group did not exceed ±1.00 mm. Hg (Schiøtz) during the period of study (table 1 and graph 1).

There was a progressive gradual fall of intraocular pressure in normal individuals first noted after the first hour and reaching the maximum on the sixth hour after the administration of the drug. This is true whether the initial dose was 50, 100 or 150 mg. (table 1 and graph 1).

In the glaucomatous subjects 100 and 150 mg. doses produced a gradual progressive

TABLE 1

AVERAGE HOURLY CHANGE IN INTRAOCULAR PRESSURE IN NONGLAUCOMATOUS AND GLAUCOMATOUS EYES WITH OR WITHOUT HYDROCHLOROTHIAZIDE BY MOUTH

Diagnosis	No. of Patients	No. of Eyes	Dosage (mg.)	P_1*	P_2*	P_3*	P_4*	P_5*	P_6*
Nonglaucomatous	14	21	None, Controls	0.00	+0.62	+0.48	+0.85	+0.43	−0.05
Nonglaucomatous	28	45	50	−0.58	−0.78	−1.51	−1.09	−1.73	−2.00
Nonglaucomatous	10	14	100	−1.57	−2.29	−2.57	−2.92	−2.79	−2.84
Nonglaucomatous	7	9	150	−0.77	−0.33	−1.55	−2.33	−2.00	−2.55
Glaucomatous	11	15	50	−2.40	−2.93	−4.60	−5.30	−6.46	−6.73
Glaucomatous	13	21	100	−1.95	−2.81	−3.14	−3.81	−2.66	−2.57
Glaucomatous	13	21	150	−1.52	−2.14	−3.19	−3.62	−2.86	−2.29

* P_1, P_2, P_3, P_4, P_5, P_6 indicates average hourly change in intraocular pressure in mm.Hg (Schiøtz) at the end of one, two, three, four, five and six hours.

TABLE 2

PERCENTAGE OF NONGLAUCOMATOUS AND GLAUCOMATOUS CASES THAT SHOWED LOWERING OF INTRAOCULAR PRESSURE WITH HYDROCHLOROTHIAZIDE BY MOUTH

Diagnosis	No. of Patients	No. of Eyes	Dosage mgms.	%1*	%2*	%3*	%4*	%5*	%6*
Nonglaucomatous	28	45	50	36	44	51	55	55	62
Nonglaucomatous	10	14	100	65	57	57	78	78	78
Nonglaucomatous	7	9	150	11	55	44	67	44	55
Glaucomatous	11	15	50	67	67	73	73	87	87
Glaucomatous	13	21	100	52	52	67	67	57	57
Glaucomatous	13	21	150	57	52	62	67	62	57

* %1, %2, %3, %4, %5, %6 indicates the percentage of cases in the various groups of patients that show a owering of intraocular tension at the end of one, two, three, four, five and six hours.

fall in intraocular pressure, starting at the first hour and reaching the maximum on the fourth hour, after which a gradual rise appeared. The lowest average fall of the intraocular pressure did not exceed 4.0 mm. Hg (Schiøtz) (table 1 and graph 2).

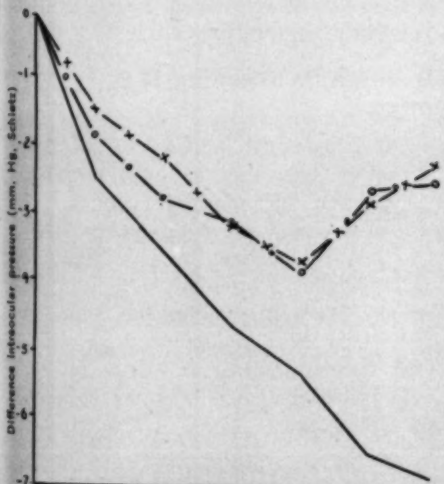
The glaucoma cases that received only 50 mg. showed, paradoxically, a greater fall in intraocular pressure beginning at the first hour and extending up to the sixth hour. At the end of the test the group showed a low average of nearly 7.0 mm. Hg (Schiøtz) fall.

Fifty percent or more of the glaucomatous cases showed a lowering of the intraocular pressure during the entire six hours of study while in the nonglaucomatous eyes there was a general delay of an hour (table 2).

Tonographic studies three hours after the administration of the drug showed variable results in normal and glaucomatous eyes and we therefore conclude that the drug had no characteristic effect on the aqueous outflow as was found similarly with chlorothiazide.[5]

No changes in the size of the pupils were seen. No ocular congestion or pain during the systemic administration of the drug was noted.

No untoward systemic effects relative to the medication were experienced by the patients. However, diuresis was stimulated in most of the cases.



Graph 2 (Fajardo, Hamilton and Leopold). Hourly changes in intraocular pressure of glaucomatous eyes (average) from 9:00 A.M. to 3:00 P.M. (———, 50 mg., o-o-o-o-, 100 mg., x-x-x-x-, 150 mg.)

MECHANISM OF ACTION

From these findings we believe that the effect of the oral ingestion of this drug on intraocular pressure must be on the production of the aqueous. It can not be due to its weak carbonic anhydrase inhibiting property for chlorothiazide which is nine times as potent as this drug in this respect did not lower the intraocular pressure.[5] The studies on the effect of this drug on the potassium and sodium contents of the aqueous attest that it produces an insignificant inhibition of the carbonic anhydrase in the ciliary body of the rabbits.[2] It is possible that the fall in the

intraocular pressure is secondary to the hypotensive and diuretic effects of the drug.

Conclusion

Oral administration of hydrochlorothiazide (Esidrex), a powerful diuretic and an effective hypotensive drug, in single doses of 50 to 150 mg. produced a slight decrease in intraocular pressure in nonglaucomatous and glaucomatous eyes of humans. Its use primarily for the control of glaucoma is not recommended because its ocular hypotensive effect is small compared to that obtained with other effective orally administered agents like acetazolamide[1] and dichlorphenamide.[6]

1601 Spring Garden Street (30).

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PHOTOALLERGIC KERATOCONJUNCTIVITIS*

K. Ullerich, M.D., K. Wulf, M.D. and A. Wiskemann, M.D.
Hamburg, Germany

In inflammatory processes of the anterior eye segment, especially in those involving conjunctiva and cornea, usually certain symptoms of dazzling may result from the patient's exposure to normal solar radiation, without the clinical picture being considerably influenced or profoundly impaired by the effect of electromagnetic waves. However, in intense radiation, such as for instance produced by reflection from snow fields, the near ultraviolet of sunlight leads to reversible lesions of the corneal and conjunctival epithelium corresponding to the symptoms of photoelectric keratoconjunctivitis.

So far, little attention has been paid to the fact that under the influence of substances formed endogenously or induced exogenously, severe inflammatory symptoms may arise at the anterior eye segment in individual cases, if the patient is exposed to normal solar radiation or even only to light at overcast sky. We want to outline this clinical picture which we have described as photoallergic keratoconjunctivitis (Ullerich, Wulf, and Wiskemann, 1957), in the light of a new observation.

Case report

H. H., a registered nurse, record number 24461/1957, now 53 years of age, had been assigned to duty on dermatologic and surgical wards since 1934. In 1940, she noticed for the first time a hypersensitivity to a hand disinfectant and to iodine solution. In 1947, a contact dermatitis of the hands occurred after dispensing sulfonamide tablets, while shortly there-

* From the University Eye Clinic (Director: Prof. Dr. H. Sautter) and from the Dermatological Clinic of the University (Director: Prof. Dr. J. Kimmig).

after sulfonamide treatment of a bronchopneumonia caused a severe, generalized exanthema.

After the skin reaction had subsided, the nurse noticed in winter 1947/48 that the skin of her face and hands became irritated as soon as she was exposed to sunlight for a while. In the spring of 1948, there was a comparative decrease in the cutaneous irritating symptoms, while a severe bilateral inflammatory condition of conjunctiva and cornea developed which showed pronounced exacerbation whenever the patient had stayed in the open air for some time.

The attempts which were made during the following two years to influence the process with astringents, antibiotics and cortisone preparations, were unsuccessful. Therapeutic efforts in several clinics failed to restore the patient's ability to work. Acute allergen tests performed in 1950 turned out to be negative.

Because of a profound corneal ulceration, spontaneous perforation of the cornea occurred in the right eye in 1950 and in the left eye in 1953. Bilaterally the anterior chamber was restored. The corneal process, however, did not heal up, so that a bilateral keratoplasty became necessary in 1954. While the transplants remained comparatively clear, new infiltrates occurred at the corneal marginal parts within the palpebral fissure on slight exposure to light.

When the patient was referred to us in 1957, she had been sick and unable to work already for eight years and she had been staying only in entirely darkened rooms for the past four years. Repeated efforts to prevent the inflammatory symptoms by wearing protective sunglasses were not successful. The inevitable short stay outdoors during the trip to Hamburg caused a severe inflammatory exacerbation of the corneal lesions.

Physical findings. On March 26, 1957, examination showed marked spotted erythema involving the cutaneous areas of hands and face not covered by clothing. Photophobia was so extreme that examination could be performed only after instillation of an anesthetic. There was bilateral reddening of the lid integument. The conjunctiva presented strong injection in the area of the palpebral fissure with cicatricial changes temporal to the corneal limbus on each side.

In the marginal parts of the lower two thirds of the cornea there was bilateral superficial infiltration with spotlike solidification in particular sectors. The infiltrates penetrated into the upper half of the substance proper of the cornea, while the deeper layers were not involved. The marginal parts of the cornea presented superficial vascularization.

In the cornea, bilaterally, was a level engrafted transplant six mm. in diameter. On the right side the center was clear, on the left there were peripheral opacities limited to the lower half of the graft. The upper area of the cornea normally covered by the upper lid was completely free from infiltrations bilaterally (fig. 1). On each side there were several punctate posterior synechias of the pupillary margin. Lenses were free from opacities. There was moderate destruction of the vitreous network. A myopic crescent encircled each disc. The retina was distended at the posterior pole and revealed the formation of myopic arcades in the periphery.

Vision was: R.E., −11.0D. sph. ⊃ −6.0D. cyl. ax. 150° = 5/15; L.E., −12.0D. sph. ⊃ −6.0D. cyl. ax. 145° = 5/20.

Discussion

Foremost among our clinical considera-

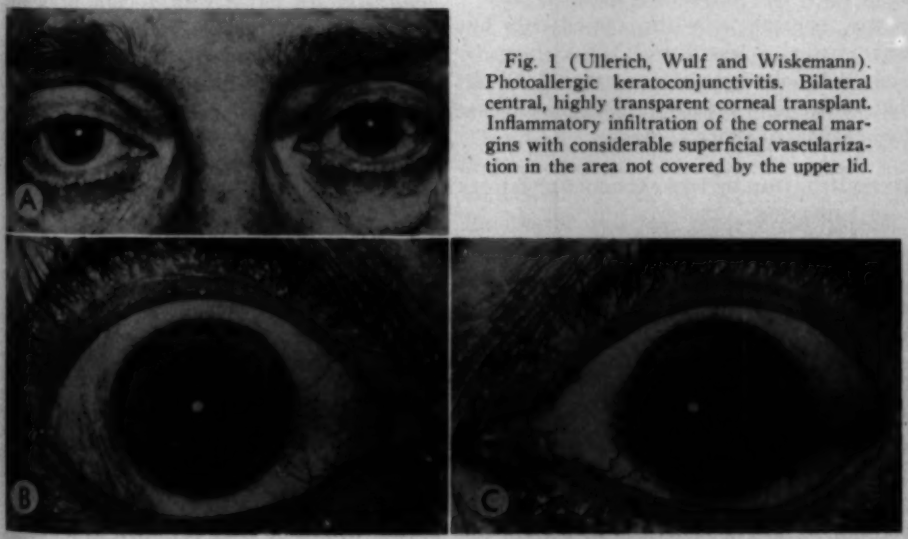

Fig. 1 (Ullerich, Wulf and Wiskemann). Photoallergic keratoconjunctivitis. Bilateral central, highly transparent corneal transplant. Inflammatory infiltration of the corneal margins with considerable superficial vascularization in the area not covered by the upper lid.

tions was the opinion that the process must have been caused by the electromagnetic radiation of the sun, that is, that a hypersensitivity to light of a definitive wavelength must be present. Furthermore, it had to be considered whether the symptoms of hypersensitivity really did affect the ocular process.

Spectral pattern and the biologic efficiency of sunlight

In order to explain the results of our tests in more detail, a short review of the spectral distribution of sunlight is presented.

The spectrum of sun and sky which arrives at the surface of the earth extends from λ ca. 2.900 Å to 30.000 Å with its maximum at 5,000 Å. Wavelengths of less than 2,900 Å are qualified as far ultraviolet, from 2,900 to 3,900 Å as near ultraviolet, from 3,900 to 7,600 Å as visible light and those of more than 7,600 Å as infrared light. If the erythema threshold determined at the skin is multiplied wavelength by wavelength with the relative intensities radiated from sun and sky to a horizontal surface we obtain the curve of spectral solar efficiency to produce erythema as shown in Figure 2.

In accordance with cutaneous sunburn (λ 2,900-3,200 Å = sunburn spectrum), photoelectric ophthalmia is also caused only by wavelengths of less than 3,200 Å. In general, ultraviolet light of more than 3,200 Å and visible light do not produce inflammatory changes of skin and eyes.

Determination of the pathogenic range of radiation

Contrary to sunburn, endogenous and exogenous solar exanthemas are caused mostly by near ultraviolet light of more than 3,200 Å as demonstrated in former studies (Wiskemann and Wulf, 1956, 1957; Schultz, Wiskemann and Wulf, 1956). The experimental technique mentioned in these studies was also employed in the present case. Assuming that the pathogenous range of radiation would be the same for the skin as for the eye, we hoped to find, with the aid of

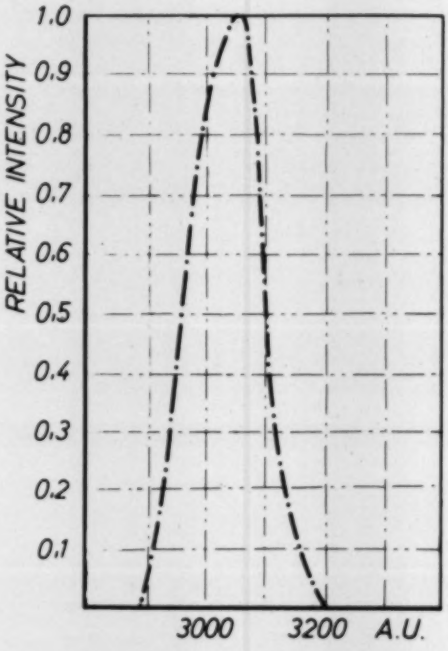

Fig. 2 (Ullerich, Wulf and Wiskemann). Sunburn spectrum (2,900 to 3,200 Å).

the results from cutaneous tests, effective filter lenses for the eyes.

At first, we tested with a high pressure mercury lamp (type S 700, quartz-lamp, Hanau), whether the inflammatory changes might eventually be based on cutaneous hypersensitivity to radiation of less than 3,200 Å which produces erythema in persons with normal sensitivity. However, the erythema threshold of the patient was within normal limits.

The effect of near ultraviolet and of visible light was tested with a source of radiation having a continuous spectrum in this particular range, the distribution of energy within the spectrum corresponding to that of sun and sky at a solar altitude of 37 degrees (Xenon high pressure lamp XBF 6000, Osram).

The distance was selected in such a way that the intensity of irradiation also corresponded to that of solar radiation in a cloud-

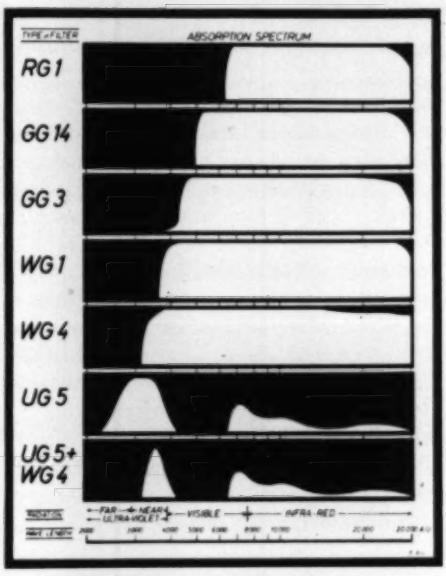

Fig. 3 (Ullerich, Wulf and Wiskemann). Spectral permeabilities of the absorption filters WG4 to RG1 which extinguish varying wave ranges from the short-wave region of the spectrum. With the filter types UG5 and WG4 combined, only near ultraviolet and infrared are allowed to pass. If no reaction takes place behind the filter RG1, a reaction behind the filter combination UG5 and WG4 can be set free only by near ultraviolet.

less sky, free horizon and at a solar altitude of 37 degrees.

In order to test electively the particular ranges of radiation, a set of absorption filters (Schott and Company, Mainz) was placed between the source of radiation and the dorsal skin. These filters permit elimination of greater and greater wave ranges from the short wave region of the spectrum toward the long-wave region of visible light (fig. 3). On an area of 4.0 by 4.0 cm. in size and with a filter thickness of 2.0 mm., a strong cutaneous erythema occurred under the filters WG4 and WG1, while a moderate erythema was produced under filter GG3 (table 1). The filters GG14 and RG1, however, prevented all cutaneous reactions.

In another test, a cutaneous field was covered simultaneously with the filter WG4 which extinguishes wave ranges up to 3,200 Å and with the filter UG5 which extinguishes in the reserve direction and has two maxima of permeability in the red toward ultrared. It could be demonstrated hereby that in the patient the noxious range of radiation within the ultraviolet was entirely confined to the long-wave region, that is, to the ultraviolet above 3,200 Å.

While under the high pressure mercury lamp, the erythema threshold was normal in our patient, a cutaneous erythema was produced by near ultraviolet above 3,200 Å and by visible light up to a wave range of 4,200 to 5,000 Å, that is, by a spectral range which does not cause inflammatory reactions of the skin in persons with normal sensitivity.

Further cutaneous tests

Before the onset of the ocular symptoms, the patient had suffered from a contact dermatitis due to a hand disinfectant, iodine solution, and sulfonamides, as well as from a drug exanthema caused by sulfonamides. Therefore, epicutaneous tests were performed in order to exclude a common cutaneous allergy. In the epicutaneous test at the dorsal skin all professional noxious agents which the nurse could have possibly

TABLE 1*

Cutaneous erythema reactions under Xenon high pressure lamp with different absorption filters

(The control test shows a retrogression of the noxious wave-range toward near ultraviolet Reading after seven hours.)

	WG 4	WG 1	GG 3	GG 14	RG 1	UG 5
March 28, 1957	+	+	(+)	ϕ	ϕ	+
July 23, 1958	+	(+)	ϕ	ϕ	ϕ	(+)

* See also Figure 3.

contacted on dermatologic and surgical wards, including particularly the substances already mentioned, proved to be negative.

At the examination for photoallergic effects of the individual substances, the test fields were irradiated with the unfiltered Xenon high pressure lamp after 24 hours. The dose amounted to one fourth of the erythema threshold. This resulted in a slight erythema in the test fields with hydroquinone and with 10-percent chlorpromazine, while the areas of all other substances did not show any reaction.

Possible causes of a hypersensitivity

In ophthalmic bibliography there are no specific references as to the classification of the clinical hypersensitivity to near ultraviolet and to visible light. During the past decades, however, dermatology has been dealing sufficiently with the problem of actinic irritations so that guiding principles regarding the classification of the ocular findings could be obtained from this specialty.

1. Endogenous solar dermatoses

For the most part, chronic polymorphous solar exanthemas exist from early childhood. Solar urticaria and porphyrin dermatoses manifest themselves by the formation of wheals and blisters under the influence of light.

Corneal involvement in porphyria has been described by Berglund, Kornerup and Paul (1955). In two patients, the authors were able to relieve considerably the irritating symptoms by prescribing filter lenses (type Noviol) which extinguish radiation of less than 4,500 Å.

2. Exogenous photodynamic reactions

a. *Phototoxic reactions.* According to Epstein (1939) and Burckhardt (1941) the term is applied to reactions which are caused by phototoxic agents, that is, to inflammatory processes which occur obligatory in every person, if photodynamically effective substances, after being induced exogenously or internally, are deposited in the skin and exposed to light. With elimination of the noxious agent photosensitivity also subsides.

Derivates of coal tar, acridine dyes, eosin and furocumarins are known to produce those effects.

b. *Photoallergic reactions.* Among photoallergic reactions are classified inflammatory processes which occur in a few, especially susceptible, persons after contact with, often very small amounts, particular substances and after subsequent exposure. Photoallergens described have been: sulfonamides (Epstein, 1939: Blum, 1941; Burckhardt, 1941), the oral drugs for diabetes, such as N-sulfanilyl-N′-butylcarbamide (Burckhardt, 1957; Schwartz, Speck 1957; Schreus and Ippen, 1958); substances from the group of phenothiazines (Sidi, Hincky and Gervais, 1955; Hiob and Hippius, 1955; Schulz, Wulf and Wiskemann, 1956; Cahn and Levy, 1957) and the blancophores (Burckhardt, 1955).

Discussion

In the past history of our patient it was pointed out that the inflammatory exacerbations on the cornea, the conjunctiva and the unprotected cutaneous areas were clearly dependent on exposure to light of normal intensity, particularly to direct solar radiation. Thus a solar dermatosis with ocular involvement was to be suspected.

By testing the effect of particular ranges of radiation at the dorsal skin it could be established that the sensitivity to wave ranges of less than 3,200 Å was normal, while a pathologically increased cutaneous sensitivity to ultraviolet of more than 3,200 Å and to visible light of 4,200 to 5,000 Å was evident, that is, hypersensitivity to a spectral range of radiation which does not cause inflammatory reactions in normal persons.

On the cutaneous morphology as well as by laboratory examinations, particularly because of the absence of porphyrinuria, an endogenous solar dermatosis could be excluded.

There was no evidence of a phototoxic

reaction in our patient, as appropriate noxious agents were not established in the past history. Furthermore, the process took an extremely chronic course. On the basis of the character of the clinical findings, on the clinical course, and on a photosensitivity existing for a period of over nine years, the process was classified as a photoallergic reaction.

The slightly positive result of the epicutaneous photodynamic test after application of hydroquinone and megaphen could not be considered as definitely pathogenic, as in the applied concentrations these substances may produce a positive cutaneous reaction in some persons with normal sensitivity. Moreover, the patient had not had any contact with hydroquinone to the best of her knowledge and her illness preceded by many years dispensing of phenothiazines for use in human medicine.

According to the past history, undoubtedly a sensitization to sulfonamides was present in 1947. As this group of substances is known to exert a photosensitizing effect, the ocular affection could have been caused by a chemical compound of this group. However, as the epicutaneous photodynamic test at the dorsal skin of the patient failed to produce a reaction after the application of sulfonamide solutions, it had to be presumed that the photoallergic reaction was no longer bound to the sulfonamide but possibly to a sulfonamide-protein complex which had been deposited in the cutis, the conjunctiva, and the cornea and which was not eliminated by metabolism during the course of the years.

Previous case

The present case shows many parallelisms to our first observation of a photoallergic keratoconjunctivitis which occurred in a 42-year-old diver who had returned to Germany from South America because of pulmonary tuberculosis. After photoallergization by N- (3'dimethylamino-propyl) -3-chlorphenothiazine a most severe bilateral keratoconjunctivitis developed in this patient, accompanied by a moderate dermatitis involving the unprotected cutaneous areas of the face and the hands. Even with an overcast sky, the sensitivity to sunlight was so high that the doctors who had previously treated the patient had to perform bilateral closure of the palpebral fissures. With the method mentioned above, we were also able to determine in this case a cutaneous hypersensitivity to radiation of λ 3,200 to 5,000 Å, that is, to a spectral range which, even at intensive solar radiation, does not cause lesions in persons with normal sensitivity.

No treatment was known which would enable us to relieve within a short time a photoallergic reaction by causal therapeutic measures. Therefore, our main task was to withhold the determined pathogenic range of radiation from the affected tissues and thus effect a cure of the inflammatory process. While in dermatology, therapeutic efforts have been made with absorbent ointments and solutions for years past, we found during our first observation that the filter glasses used for the testing were suitable for symptomatic treatment of the severe ocular process.

By means of filter glasses we were able to relieve entirely this patient's complaints, to effect a cure of the cornea and to re-open the palpebral fissures. Later on, while employed at the port of Hamburg, he always remained free from relapses, although he had to work in the open air and frequently under intensive solar radiation.

Having in mind the previous case just described, special spectacles with close-fitting side protections were fitted to our present patient. First the correcting lenses for high myopia and myopic astigmatism were fixed in the spectacle frame. To this frame front lenses containing the filters RG1 and GG14 were fitted so that they would be impervious to light (fig. 4). The first correction provided entire relief from complaints, even when the patient was exposed to bright light for several hours. Of course, she had to put up with the loss of the chromatic scale of the short-wave region of the spectrum to a great extent. Under overcast skies and while staying indoors, the filter GG14 proved to be sufficient and was preferred because it merely eliminated the region of radiation belonging to violet and blue.

Under treatment with these filter glasses, the photoallergic keratitis subsided completely within four days. The infiltrates at the corneal marginal area disappeared, and vascularization diminished. Vision of the left eye improved to 20/40 by resorption of the infiltrates at the corneal transplant. A short relapse could be eliminated instantly by replacing the lateral part of the spectacles.

The patient's eyes had been affected for more than nine years. She had not been able to work as a nurse for eight years and she

Fig. 4 (Ullerich, Wulf and Wiskemann). Photoallergic keratoconjunctivitis. Special spectacles employed: side protection impervious to light. Because of myopia the necessary concave lenses are fitted into the frame, above them light-protecting front lenses with filters RG1 GG14, respectively.

had been staying only in darkened rooms for four years. Today, after wearing the spectacles for 18 months, she is completely relieved of her complaints, is working in a nurses' home, and is able to stay in the open air for hours. The cutaneous irritating symptoms also subsided under symptomatic treatment, that is after the filter glasses had been provided.

A control examination performed 16 months after the beginning of treatment revealed that the photosensitivity had retrogressed to a certain extent. The erythema threshold of the skin shifted to the short-wave range of visible light from 4,200 to 5,000 Å toward 3,700 to 4,200 Å. In accordance with these results the nurse was also able to get along with the filter GG14 in sunlight and to wear the filter GG3 under overcast skies as well as indoors. Since the GG3 filter is almost achromatic, it is not resented for cosmetic reasons, it merely eliminates the shortest wave range of visible light.

Summary

A bilateral inflammatory process involving the cornea and conjunctiva is described as photoallergic keratoconjunctivitis. In a 53-year old nurse, inflammatory symptoms of the skin, as well as of the conjunctiva and cornea developed, probably after cutaneous and parenteral sensitization by sulfonamides. These symptoms were relapsing whenever the patient was exposed to slight solar radiation. All therapeutic efforts during nine years yielded negative results. Because of bilateral corneal ulceration with perforation and temporary drainage of the anterior chamber, keratoplasty became necessary.

When the patient was admitted for treatment, she had been unable to follow her profession for eight years and had been staying only in darkened rooms for four years to avoid any exacerbation of her condition from exposure to light.

By determination of the pathogenic wave ranges on the dorsal skin it was established that the erythema threshold was not decreased under the high pressure mercury lamp. However, abnormal sensitivity to ultraviolet above 3,200 Å and to the short-wave region of visible light was present. With the past history in mind, the process was interpreted as photosensitization to the sulfonamides applied before the onset of the clinical picture.

By protecting both eyes with filter glasses impervious to the pathogenic region of radiation we succeeded without special therapeutic measurements to relieve the patient's complaints entirely and to restore her ability to work. At a control examination the pathogenic region of radiation for cornea and skin showed a retrogression toward the short wave range of visible light. Therefore, further desensitization is to be expected over the years.

Martinistrasse 52.

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THERAPEUTIC STUDIES IN EXPERIMENTAL CHEMICAL INJURY OF THE CORNEA*

II. Phosphate buffer (Neutralize) studies

Gustav C. Bahn, M.D., Earl Sonnier, M.D., and James H. Allen, M.D.
New Orleans, Louisiana

The concept of counteracting the effects of noxious agents when applied to the cornea and conjunctiva by neutralization is not new. Basic solutions such as sodium bicarbonate and aluminum hydroxide have been applied to eyes burned with acids and conversely, very dilute solutions of acetic and even hydrochloric acids have been used in alkali burns of the cornea without particularly striking benefit. Buffering the action of noxious agents with such chemical buffers as neutral ammonium tartrate has yielded only limited results.

An ideal neutralizing or buffering agent should (1) be capable of promptly combining with any of the common mineral acids and alkalis; (2) maintain a pH in the neighborhood of 7.2; (3) be nontoxic and nonirritating; (4) be an aqueous solution easily preserved and effective in relatively small amounts.

This investigation is part of a systematic survey of therapeutic agents to determine the most effective method of managing acute corneal chemical injuries.

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A relatively new agent, Neutralize, consisting of a monobasic potassium phosphate and dibasic sodium phosphate buffer solution, having a molarity of 0.5, was employed as a first-aid procedure in the management of representative acid and alkali corneal burns in the experimental animal. The effectiveness of the drug was compared with distilled water, the most common irrigant now in use.

Albino rats of the Wistar strain were used as the experimental animal. The burns were induced with sulfuric acid, nitric acid, and sodium hydroxide, the splash technique of injuring the eyes being employed. Evaluation of the course of the burns was made by periodic slitlamp examination, and data were computed according to our own modification of the Friedenwald scheme of evaluating corneal injuries. The burn technique and statistical evaluation of the data were essentially the same as previously reported in Part I† of this study.

Experimental results

Experiment I

Bilateral corneal lesions were induced in 15 albino rats with 1 N sodium hydroxide. The right eyes were promptly irrigated for one minute with Neutralize. The left eyes were irrigated with distilled water for one minute. The results are seen in Table 1.

Conclusions. No significant difference in healing rate and final state of the cornea could be noted between eyes treated with Neutralize and those treated with distilled water after having been burned with 1 N sodium hydroxide solution.

Experiment II

Standard burns of both eyes of 15 albino rats were produced with 1 N hydrochloric acid. The right eyes were irrigated with Neutralize for one minute. The left eyes were similarly irrigated with distilled water for one minute. Results are tabulated in Table 2.

Conclusions. No significant difference in healing rate and final state of the cornea could be noted between eyes treated with Neutralize and those treated with distilled water after having been burned with 1 N hydrochloric acid.

Experiment III

Bilateral corneal burns were produced in 15 albino rats with 1 N hydroxide solution. The right eyes were irrigated with Neutralize for five minutes. The left eyes were similarly irrigated with distilled water for five minutes. The results are shown in Table 3.

Conclusions. No significant difference in healing rate and final state of the cornea could be noted between eyes treated with Neutralize and those treated with distilled water after having been burned with 1 N sodium hydroxide solution.

† Bahn, G. C., and Allen, J. H.: Therapeutic studies in experimental chemical injury of the cornea: 1. Calsulfhydryl studies. A.M.A. Arch. Ophth., **52**: 22-27, 1955.

TABLE 1

Comparison of Neutralize-treated right eyes with untreated left eyes following standard burn of each eye with 1.0 N sodium hydroxide solution

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	22.99	23.33	+0.34	1.12	0.30
48	22.46	22.40	−0.06	0.10	0.90
72	22.53	22.46	−0.07	0.08	0.90
120	29.06	30.73	+1.66	2.38	0.05
144	29.93	31.93	+2.00	2.14	0.05
168	30.60	28.40	−2.20	2.81	0.02
192	27.86	29.66	+1.80	3.48	0.01
216	27.80	28.26	+0.46	1.14	0.30

TABLE 2

COMPARISON OF NEUTRALIZE-TREATED RIGHT EYES WITH UNTREATED LEFT EYES FOLLOWING STANDARD BURN OF EACH EYE WITH 1 N HYDROCHLORIC ACID

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	0.46	2.66	+2.20	2.94	0.02
48	1.13	2.53	+1.40	1.99	0.10
72	0.46	1.33	+0.86	1.76	0.10
96	0.00 mm.	0.28	+0.28	1.11	0.30
144	0.00	0.00	0.00	0.00 mm.	1.00

TABLE 3

COMPARISON OF NEUTRALIZE-TREATED RIGHT EYES WITH UNTREATED LEFT EYES FOLLOWING STANDARD BURN OF EACH EYE WITH 1 N SODIUM HYDROXIDE SOLUTION

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	23.86	23.53	−1.33	2.62	0.02
48	24.33	23.86	−0.46	0.89	0.40
72	23.26	23.46	+0.19	0.29	0.80
96	22.80	23.20	+0.40	0.59	0.60
144	26.66	26.53	−0.13	0.19	0.90
168	28.20	28.00	−0.20	0.32	0.80
192	27.53	27.13	−0.40	0.79	0.50
216	27.66	27.53	−0.13	0.28	0.80
288	27.66	27.53	−0.13	0.28	0.80

TABLE 4

COMPARISON OF NEUTRALIZE-TREATED RIGHT EYES WITH UNTREATED LEFT EYES FOLLOWING STANDARD BURN OF EACH EYE WITH 2 N NITRIC ACID SOLUTION

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	8.80	8.73	−0.07	0.07	0.90
48	4.66	5.33	+0.66	0.96	0.40
72	2.66	2.46	−0.20	0.79	0.50
96	0.40	0.60	+0.20	0.56	0.60
144	0.00	0.00	0.00	0.00	1.00

EXPERIMENT IV

Both eyes of 15 albino rats were burned with 2 N nitric acid. The right eyes were irrigated with 50 cc. of Neutralize. The left eyes were similarly irrigated with 50 cc. of distilled water. The results are shown in Table 4.

Conclusions. No significant difference could be noted in the healing rate or the amount of residual scarring of albino rat corneas when treated with Neutralize as compared with distilled water, after having been burned with 2 N nitric acid.

EXPERIMENT V

Standard corneal burns were produced in both eyes of 15 albino rats with 1 N sodium hydroxide solution. The right eyes were promptly irrigated with 50 cc. of Neutralize. The left eyes were irrigated with 50 cc. of distilled water. The results are shown in Table 5.

Conclusions. No significant difference was noted between the eyes treated with 50 cc. of Neutralize and those treated with 50 cc. distilled water after having been burned with 1 N sodium hydroxide solution.

TABLE 5

COMPARISON OF RIGHT EYES TREATED WITH NEUTRALIZE (50 CC.) AND LEFT EYES TREATED WITH 50 CC. OF DISTILLED WATER FOLLOWING STANDARD BURNS OF EACH EYE WITH 1 N SODIUM HYDROXIDE SOLUTION

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	18.93	19.66	+0.67	2.45	0.05
48	20.00	20.86	+0.86	1.57	0.20
72	19.40	21.40	+2.00	3.09	0.01
96	17.73	19.93	+2.20	3.57	0.01
144	16.73	17.60	+0.86	1.03	0.30
192	13.86	15.12	+1.26	1.35	0.20
240	10.86	11.00	+0.13	0.29	0.80

EXPERIMENT VI

Both eyes of 15 albino rats were burned with 2 N nitric acid. The right eyes were treated with three drops of Neutralize. The left eyes were similarly irrigated with three drops of distilled water. The results are shown in Table 6.

Conclusions. Rat eyes burned with 2 N nitric acid and treated with minute amounts of Neutralize healed significantly faster and with less residual scarring than did similarly burned eyes treated with minute amounts of distilled water.

EXPERIMENT VII

Both eyes of 15 albino rats were burned with 1 N sodium hydroxide solution. The right eyes were treated immediately with three drops of Neutralize. Three drops of distilled water were instilled into the left eyes. The results are shown in Table 7.

Conclusions. Rat eyes burned with 1 N sodium hydroxide solution and treated with small amounts of Neutralize healed more rapidly and with less residual scarring than did similarly burned eyes irrigated with small amounts of distilled water.

EXPERIMENT VIII

The corneas of 15 albino rats were burned with 1 N sodium hydroxide solution. The right eyes were promptly irrigated with three drops of Neutralize. The left eyes received no treatment, serving as controls. The results are shown in Table 8.

Conclusions. The eyes of experimental animals treated with small amounts of Neutralize after having been burned with 1 N sodium hydroxide solution healed signficantly faster and with less residual scarring than did similarly burned completely untreated eyes.

EXPERIMENT IX

Standard corneal lesions were produced by 2 N nitric acid in 15 rats. The right eyes were treated with three drops of Neutralize. The left eyes received no treatment thus

TABLE 6

COMPARISON OF RIGHT EYES TREATED WITH THREE DROPS OF NEUTRALIZE AND LEFT EYES TREATED WITH THREE DROPS OF DISTILLED WATER FOLLOWING STANDARD BURNS OF EACH EYE WITH 2 N NITRIC ACID

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	6.80	14.60	+7.80	11.17	0.00
48	4.66	13.40	+8.73	11.38	0.00
72	3.33	10.80	+7.46	11.68	0.00
96	1.20	8.73	+7.53	13.26	0.00
144	0.00	7.33	+7.33	11.92	0.00

TABLE 7

COMPARISON OF RIGHT EYES TREATED WITH A MINUTE AMOUNT OF NEUTRALIZE AND LEFT EYES TREATED WITH AN EQUALLY SMALL AMOUNT OF DISTILLED WATER FOLLOWING STANDARD BURNS OF EACH EYE WITH 1 N SODIUM HYDROXIDE SOLUTION

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	19.46	25.40	+ 5.93	6.78	0.00
48	20.00	26.66	+ 6.66	7.75	0.00
72	18.93	26.88	+ 7.89	7.95	0.00
96	18.66	27.33	+ 8.88	10.24	0.00
144	18.00	29.33	+11.33	14.58	0.00
192	16.40	30.00	+13.60	15.66	0.00
240	12.96	30.11	+17.14	19.48	0.00

TABLE 8

COMPARISON OF RIGHT EYES TREATED WITH SMALL AMOUNTS OF NEUTRALIZE AND LEFT UNTREATED CONTROL EYES FOLLOWING STANDARD BURNS OF EACH EYE WITH 1 N SODIUM HYDROXIDE SOLUTION

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	19.60	26.00	+ 6.00	6.82	0.00
48	20.00	27.00	+ 6.81	7.11	0.00
90	19.46	25.42	+ 5.95	6.81	0.00
96	18.92	26.81	+ 7.82	7.93	0.00
144	16.42	29.57	+12.87	15.21	0.00
192	14.22	30.31	+15.46	17.37	0.00
240	11.28	28.89	+18.77	18.23	0.00

TABLE 9

COMPARISON OF RIGHT EYES TREATED WITH SMALL AMOUNTS OF NEUTRALIZE AND LEFT UNTREATED CONTROL EYES FOLLOWING STANDARD BURNS OF EACH EYE WITH 2 N NITRIC ACID SOLUTION

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	16.45	31.69	+14.23	16.21	0.00
48	18.63	26.82	+ 8.20	9.11	0.00
72	18.00	30.53	+11.46	12.86	0.00
96	16.75	28.04	+11.29	12.70n	0.00
144	16.43	30.11	+13.68	14.52	0.00
192	12.91	28.55	+15.64	17.23	0.00
240	10.88	27.23	+16.35	18.31	0.00

serving as controls. The results are shown in Table 9.

Conclusions. Rat corneas burned with 2 N nitric acid healed significantly faster and with less residual scarring and vascularization than did similarly burned untreated eyes, when treated with very small amounts of Neutralize.

EXPERIMENT X

Both eyes of 15 albinos rats were burned with 2 N nitric acid. The right eyes were irrigated with 50 cc. of Neutralize containing no chlorobutanol preservative. The left eyes were irrigated with 50 cc. of distilled water. Because of the reported inhibitory effect of chlorobutanol upon epithelial healing, several experiments were conducted using the phosphate buffer solution without any preservative (table 10).

Conclusions. Rat eyes burned with 2 N

TABLE 10

COMPARISON OF RIGHT EYES TREATED WITH 50 CC. OF NEUTRALIZE CONTAINING NO CHLOROBUTANOL PRESERVATIVE AND LEFT EYES TREATED WITH 59 CC. OF DISTILLED WATER FOLLOWING STANDARD BURNS OF EACH EYE WITH 2 N NITRIC ACID

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	7.20	6.73	−0.46	0.92	0.40
48	3.80	3.56	−0.33	0.68	0.50
72	1.86	1.66	−0.20	1.03	0.30
96	0.40	0.20	−0.20	1.03	0.30
144	0.00	0.00	0.00	0.00	1.00

TABLE 11

COMPARISON OF RIGHT EYES TREATED WITH 50 CC. OF NEUTRALIZE CONTAINING NO CHLOROBUTANOL PRESERVATIVE AND LEFT EYES TREATED WITH 50 CC. OF DISTILLED WATER FOLLOWING STANDARD BURNS OF EACH EYE WITH 1 N SODIUM HYDROXIDE SOLUTION

Hours Following Injury	Average Score Treated Eyes	Average Score Control Eyes	Average Difference	t	P
24	19.13	18.86	−0.26	1.31	0.30
48	m20.13	19.40	−0.74	3.73	0.01
72	19.60	19.13	−0.46	1.74	0.20
96	18.40	17.93	−0.46	1.92	0.20
144	17.73	17.60	−0.13	0.68	0.50
192	14.86	15.00	+0.59	0.59	0.50
240	11.33	11.66	+0.33	0.96	0.30

nitric acid healed at the same rate and with the same degree of residual scarring when treated with a phosphate buffer solution containing no preservative as did similarly burned eyes treated with an equal amount of distilled water.

EXPERIMENT XI

Standard burns were produced in both eyes of 15 albino rats with 1 N sodium hydroxide solution. The right eyes were irrigated with 50 cc. of Neutralize containing no chlorobutanol preservative. The left eyes were irrigated with 50 cc. of distilled water. The results are shown in Table 11.

Conclusions. Rat eyes burned with 1 N sodium hydroxide solution and treated with 50 cc. of Neutralize containing no preservative healed at the same rate and with the same amount of residual scarring as did similarly burned eyes treated with 50 cc. of distilled water.

SUMMARY AND CONCLUSIONS

1. Prompt application of Neutralize will protect animal eyes from acid or alkali burns but the same degree of protection can be obtained with adequate irrigation of the eye with distilled water.

2. In no experiment were any detrimental effects of the buffer solution "Neutralize" encountered.

3. No difference was noted between the effect of Neutralize with and without chlorobutanol added as a preservative.

4. No significant difference was noted between Neutralize treated and untreated eyes, when Neutralize was not promptly instilled. This would indicate that, unless the buffer solution is applied immediately, it is of no value.

5. These experiments would tend to show some clinical usefulness for the phosphate buffer solution, especially as recommended for use in the field, or under conditions where water for irrigating purposes is unavailable. No superiority to adequate irrigation with distilled water was demonstrated.

1430 Tulane Avenue (12).

CARCINOMA OF THE MAXILLARY SINUS WITH OCULAR INVOLVEMENT*

Report of four cases

Jerome A. Montana, M.D., and Thomas R. Hedges, Jr., M.D.
Philadelphia, Pennsylvania

Introduction

It is the purpose of this paper to bring to the attention of ophthalmologists the importance of carcinoma of the maxillary sinus as a cause of exophthalmos and the orbital apex syndrome. The four cases in this report presented similar clinical pictures. Because of this similarity, it is hoped that something may be learned which will aid in early diagnosis in future cases.

Duke-Elder[1] states that carcinoma of the maxillary sinus is the commonest malignant disease of any of the sinuses to invade the orbit. Since the ophthalmologist may be the first physician to see these cases, we feel it is important to stress the varied signs and symptoms which may raise our index of suspicion. First and most important is involvement of the first division of the fifth cranial nerve causing uniocular pain. Paresis of the extraocular muscles is a common finding when the third, fourth, or sixth cranial nerves are affected. There may also be sympathetic nerve paresis. These signs together constitute the so-called superior orbital fissure syndrome. If the optic nerve is also involved, as is frequently the case, the term orbital apex syndrome may be applied.[2] Exophthalmos due to invasion of the orbit also occurs in varying degrees to complete the typical clinical picture.

Four cases with established pathologic diagnosis will be presented to illustrate the picture of carcinoma of the antrum as seen by the ophthalmologist.

Case reports

Case 1

A. W., a 43-year-old Negro, was admitted to the Wills Eye Hospital with a history of blurred vision and bulging of the left eye of six months' duration. He also experienced bouts of sharp left facial pain and noted numbness of the left side of the face. Examination revealed vision to be: O.D., 6/12; O.S., no light perception.

There was proptosis of the left eye straight forward with increased orbital resistance and ptosis. The left pupil was semidilated. There was a paralysis of all extraocular movements on the left with an absent corneal reflex, hypalgesia to pin prick of the left second division of the fifth cranial nerve and blockage of the left naris.

Fundus examination revealed a pale disc on the left. A small piece of polypoid tissue was visible in the left superior naris. The possibility of a gumma of the orbit was considered when the serology was reported as four plus. However, vigorous antiluetic therapy had no effect on the condition. X-ray films revealed sclerosis of the orbital bones with obliteration of the ethmoid and maxillary sinuses and apparent destruction of the left orbit.

Biopsy of the polypoid mass in the naris was reported as cystic adenocarcinoma. The patient left the hospital at his own request without therapy. Three months later he was readmitted in a comatose state with bilateral exophthalmos and died. An autopsy revealed that the tumor had extended upward into the frontal bone with a tumor mass displacing the brain to the right. There was also involvement of the left orbit, frontal sinuses, sella turcica and right anterior wing of the sphenoid.

Case 2

J. W., a 66-year-old Negro, developed blockage of the right nostril associated with pain over the entire right side of the head. A polyp was discovered in the right nasal passage and removed. Five months later he developed gradual loss of vision and was admitted to Wills Eye Hospital. The patient denied pain at the time of admission. Examination revealed no light perception in both eyes.

There was proptosis on the right with semidilated fixed pupils. (fig. 1). Ocular rotations were full. There was bilateral optic atrophy on fundus examination. A lobulated mass was discovered in the right naris including the nasal bridge and right orbital walls. X-ray studies were intrepeted as clouding of the right maxillary sinus with destruction of the medial wall and roof and invasion of the nose. A biopsy of the lesion in the right nasal fossa revealed adenocarcinoma. Radiation therapy was instituted, but the patient died at home one year later.

Case 3

E. K., a 44-year-old Negress complained of a swollen painful eye of two months' duration and was admitted for study at Wills Eye Hospital. One year

* From the Wills Eye Hospital.

Fig. 1 (Montana and Hedges). *Case 2* shows only proptosis on the right but was totally blind in both eyes.

before, she had a "dead sensation" over the left maxillary area of the face which lasted one week and cleared. This reoccurred two months before admission and was followed by pain in the left frontal and temporal regions along with proptosis of the left eye. She also noted blurred vision for two months and complained of "a stuffed left nostril."

Examination revealed vision to be: O.D., 6/9-1; O.S., 6/21-1.

There was displacement of the left globe laterally and superiorly and increased orbital resistance. An obstructed left nostril was discovered with distention of the lateral wall of the nasal cavity. This was associated with a yellow discharge.

X-ray studies showed clouding of the left ethmoid and maxillary sinuses with destruction of the floor of the left orbit. A biopsy of the lesion in the left naris showed squamous-cell carcinoma. The patient was started on radiation therapy and was unchanged two months later when last seen.

Case 4

M. C., a 50-year-old white woman, was admitted to Wills Eye Hospital with a three-month history of frontal headaches followed by swelling over the area of the left maxillary sinus and nasal discharge. There was gradually increasing proptosis and the development of nonpainful swelling along the left intraorbital area. Examination revealed proptosis of the left eye associated with complete extraocular muscle palsy, displacement of the globe upward, chemosis of the conjunctiva, lid edema, and infraorbital anesthesia (fig. 2).

X-ray films revealed diffuse clouding of the left antrum with destruction of the lateral wall and roof. A biopsy was taken from the left antrum which was interpreted as squamous-cell carcinoma.

A resection of the left maxilla and zygoma and exenteration of the left orbit were done, using a skin graft from the thigh to line the operative defect. Specimens taken at that time showed squamous-cell carcinoma extending into all sections including one from the orbital apex. The patient was given radiation therapy. Six months later the patient was noted to have local recurrence and generalized metastases and is now in a terminal state.

Discussion

These cases are illustrations of the depressing picture of carcinoma of the antrum. Two of four patients died within a year of diagnosis. Unfortunately most authorities feel that an early diagnosis is almost always accidental and when discovered the tumor is rarely confined to the antrum. These patients are often treated for varying periods of time as cases of chronic sinusitis or have no symptoms at all until the tumor has invaded adjacent structures.

Malignant tumors of the maxillary sinus are said to represent about 0.2 percent of all human cancer. It is the most frequent sinus involved (5:1). The condition is more frequent in males (4:1) in the age range of 55 to 75. Cases have been reported in children aged three years.[3] The most common type of carcinoma seen is squamous cell (approximately 90 percent) with adenocarcinoma, adenoides cysticum and transitional cell type less frequent.[4] The antrum is thin walled and easily broken through by the tumor mass, and the cribriform plate is the only barrier to intracranial extension.

Fig. 2 (Montana and Hedges). *Case 4* shows chemosis of the conjunctiva, lid edema, proptosis with displacement of the globe upward, and immobility of the globe (superior orbital fissure syndrome). This patient had infraorbital anesthesia.

If earlier diagnosis is to be made more frequently, certain symptoms and signs must be emphasized as they often seem obscure and insignificant at first observation. Such symptoms and signs include unilateral nasal discharge or nasal obstruction, epistaxis, paresthesias or anesthesias of the face, lacrimation, facial pain, diplopia, malar prominence, anosmia, ulceration of the hard palate, exophthalmos, and, in the later stages, changes in the voice or personality.

In his series of 60 cases, Tabb reported orbital invasion in 15 cases.[3] He also describes less frequent symptoms, such as convulsions with intracranial involvement.

Many patients give a history of recent nasal or dental surgery. The duration of symptoms may vary from one day to two years. One should always be suspicious of nasal polyps of long standing or purulent sinus infections not responding to therapy.[5] Patients with unilateral lacrimation require intensive investigation including examination of the nasolacrimal ducts with an opaque medium.

Duke-Elder states that the condition should be suspected whenever the ophthalmologist sees an elderly patient with epiphora and infraorbital anesthesia.[1] The symptom of infraorbital anesthesia was investigated by Waltner and Fitton[6] who felt it occurred early in the course of the disease. In their series of 38 cases of antral carcinoma, 90 percent of the cases already had bone destruction on X-ray examination; however, the four cases which were seen with infraorbital anesthesia as their first and only complaint had no bone involvement. This is illustrated in the case presented here in which the patient gave a history of infraorbital anesthesia one year before more severe symptoms led her to seek medical advice.

Exophthalmos appears frequently and therefore carcinoma of the antrum must be ruled out in all cases of unilateral exophthalmos. Walsh[2] states that the direction of displacement of the eye is important in diagnosis. If there is pronounced lateral or vertical displacement, sinus or primary orbital disease should be suspected. Gummas of the orbit usually displace the globe downward. If the direction is directly forward, the optic nerve is probably involved and there is often associated loss of vision. Increased orbital resistance may also be noted when a mass is displacing the globe. Walsh also emphasizes the fact that a tumor should be suspected whenever exophthalmos is accompanied by internal ophthalmoplegia and extraocular muscle palsies. Ward[7] noted that the lid fissure may be obliquely slanted in cases with intraorbital extension from below. Palpebral edema and chemosis may be present due to venous stasis.

One of the most important aids in diagnosis is the X-ray film. Characteristic changes include increased density of the sinuses and expansion or destruction of bone with or without irregularity of soft tissue outlines. Tabb stresses the use of radiopaque media in the sinuses, as this will often lead to earlier diagnosis. The use of orbital tomograms has also been advocated.[3]

A biopsy should always be attempted to confirm the diagnosis and to determine the type of malignancy. It should be emphasized that a negative report on a tumor which obstructs the nasal cavity is not conclusive for the anterior portion is frequently inflammatory or necrotic. Likewise aspiration biopsy and Papanicalaou studies are only of value if positive.[8] Therefore one negative biopsy does not preclude this diagnosis and a second and third biopsy often must be attempted to establish the diagnosis of malignancy.

Any discussion of the treatment of carcinoma of the antrum can only be preceded by the statement that the prognosis is gloomy in most cases in spite of modern therapy and surgical techniques. Radical surgery is felt to be of greater benefit than X-ray therapy as far as ultimate outcome and patient comfort is concerned.[9] In one series of 334 cases a combination of radiation and surgery was used in 128 while X-rays alone were used in

206.[10] The five-year survival rate with combination therapy was 45 percent while with X-ray alone it was 12 percent. Most authorities advocate surgery, with X-rays reserved for follow-up or far advanced cases.

The surgery is done in an en-bloc procedure removing the maxilla and part of the hard palate. Of interest to us is the question when the eye should be sacrificed. This may not always be ascertained until surgery is begun. Most men feel the eye should be removed when there is any clinical evidence of orbital involvement, such as decreased motility, visual loss, or X-ray evidence of orbital invasion. In such instances, exenteration is done as part of the en-block removal.[8] Split-thickness skin grafts may be used to line the operative defect. This is certainly radical surgery, yet, considering the unpleasant details of death in untreated cases with malignant cachexia, extreme pain and deformity, the risk and deformation from this type of surgery seems justified.

Summary

Four cases of carcinoma of the maxillary sinus have been presented illustrating the typical symptoms, signs, and course of the disease. It has been pointed that the prognosis is poor. Most patients are examined late or the condition is overlooked because of its obscure early course. Ophthalmologists often see the cases first because of the frequent ocular involvement. Treatment involves radical surgery with sacrifice of the orbital structures if involved.

1711 Rittenhouse Square (3).

Acknowledgment

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SURGICAL SUPPORT OF THE POSTERIOR SCLERA*

Part I. Experimental results

Brian J. Curtin, M.D.
New York

The surgical approach to the treatment of sclerectatic myopia has recently become the object of increasing interest.[1-3] Previous surgical efforts in this direction, notably lens extraction,[4] scleral shortening[5,6] and corneal flattening,[7] while correcting the refractive error to a variable extent, have been of limited value because the catastrophic chorioretinal degeneration was not prevented. This degeneration appears to be a constant accompaniment of the enlargement of the posterior segment of the globe. While the exact nature of the process by which this enlargement occurs is unknown, recent microscopic[8] and ultramicroscopic[9] evidence has strongly incriminated the sclera. The reinforcement of the posterior sclera has thereby evolved as a new approach to this important problem.

In 1951, a study was instituted at the Eye-Bank Laboratory whose object it was to develop a procedure capable of effecting such scleral reinforcement. At the outset prerequisites were apparent. These concerned both the operative procedure and the supporting material itself.

The operation

1. Inasmuch as the anterior sclera in pathologic myopia is normal, the reinforcing material may use this area as its base. In this manner, a periscleral sling, anchored anteriorly and extending about the posterior globe could render effective support to this area.

2. A minimum of trauma and complications should be encountered. Because the ectasia frequently involves the macula, a sling in this area might easily damage the posterior ciliary vessels and nerves as well as the vortices.

3. The procedure should be sufficiently versatile so that, with slight variations, maximum support may be obtained at different areas depending upon the site of the ectasia, that is the nasal sclera in myopia inversa, the inferior sclera in Von Ammon's type and the like.

4. As much sclera as possible should be supported from as many different directions as possible. A unidirectional support can effect but little reinforcement at right angles to it.

The material

1. The material should be biologically compatable with the globe and orbital contents. Materials which would produce excessive reaction, scarring or undergo rejection and absorption would be of little or no value. Also, materials which could not incorporate themselves into the supporting structure of the globe would be equally undesirable.

2. It must be sufficiently malleable. This facilitates the procedure but, more importantly, is essential in obtaining circumferential contact with the sclera.

3. It must have sufficient tensile strength, after surgery. This is dependent not only upon the innate strength of the material, but also upon the firmness of its union with the sclera and the acceptance of the material by the host.

Preliminary experiments indicated a cruciate material to be of superior design. With the intersection of the cross placed at the center of the ectasia posteriorly and the four arms reaching meridionally forward to insert into anterior sclera, effective posterior support could be expected.

Method and Materials

In order to study the accuracy of technique and possible complications of such an

* From the Laboratory of the Eye-Bank for Sight Restoration, Inc. This study was supported by a grant from the Eye Research Fund.

operative procedure, an initial series of surgical experiments were conducted. Chinchilla rabbits were used in these studies. Two untreated 4-0 braided black silk sutures tied together at the midpoints were used as the cruciate periscleral supporting material. A detailed preoperative examination, including corneal sensitivity, pupillary reactions and a tonometric tension, was conducted with postoperative progress notes and a similarly detailed antemortem examination completing the data.

The animals were killed at varying periods of one to 52 weeks postoperatively, at which time the position of the sutures, arc contact, reaction of surrounding tissues and any gross pathology were noted. The globes were fixed in Bouin's solution, embedded in paraffin, sectioned and stained with hematoxylin and eosin, Verhoeff, Van Gieson and periodic acid-Schiff stains. Microscopic studies were then conducted.

At surgery, an attempt was made to place the suture's intersection as close to the optic nerve as possible. The four "arms" were then passed meridionally forward to be sutured into anterior sclera in the four quadrants of the globe, equidistant from one another. A series of 12 experiments was conducted. It was found that the globe tolerated the procedure well, the only complication being "cage" abrasions of the cornea. This was prevented by routine suturing of the lids for 24 hours postoperatively. On post-mortem examination, the average distance of the suture intersection to the optic nerve was 2.9 mm. The arc contact was generally good. There was a very mild fibrosis about the suture but no orbital adhesions were present.

After this preliminary work, the study was then directed to the actual support of the sclera. Two methods were considered: the first had as its principle the stimulation of an adequate fibrosis about the supporting material; the second, made use of dense collagen tissue grafts, both autologous and homologous.

A number of experiments, isolated attempts as well as entire series, were performed to study the periscleral fibroblastic capabilities of various materials. The chinchilla rabbit was again the experimental animal. The results with the materials tested can be briefly summarized.

1. Tantalum, in spite of a recog zed effect,[10] produced negligible fibrosis when used in a 4-0 braided wire suture. Furthermore, its lack of malleability made it totally unsuited for this work.

2. Sodium dicetyl phosphate,[11,12] although exhibiting excellent fibroblastic effects in vascular surgery, failed to produce an adequate periscleral fibrosis. It was used in concentrations of from 0.5 to 5.0 percent in both oil and aqueous media on waxed and unwaxed twisted silk and cotton sutures. Even when applied in molten and powdered state to various suture materials, dicetyl phosphate was of little value.

3. Sodium psylliate[13,14] (Sylnasol, Searle) an otherwise effective sclerosing agent, when applied to various type sutures in the concentration of five percent was without effect.

After a total of 21 such experiments, this approach was abandoned.

In the study of dense collagen tissue grafts, the same principles and much of the same experimental routine and operative technique were used.

Again the chinchilla rabbit was the experimental animal. The same detailed preoperative, postoperative, antemortem and postmortem examinations were performed. In addition, the tensile strength of the graft at the posterior pole was ascertained in occasional unselected cases. The microscopic studies varied somewhat in that the periodic acid-Schiff was used less frequently and the acid mucopolysaccharide stain (Rinehart-Abul modification) substituted. Occasionally the Wilder reticular stain was used.

The operative technique, in detail, is as follows:

Donor fascia lata or Achilles tendon is obtained in one piece measuring some 4.0 mm.

by 60 mm. The specimen is bisected longitudinally leaving, however, a central area intact. Thus the graft material assumes a cruciate shape with spreading of the four arms. A general anesthetic (Pentothal) is used, augmented with a retrobulbar injection of two-percent procaine. A lateral canthotomy is done and lid sutures inserted. A traction suture is placed in the temporal limbus. A crescentric incision is made through conjunctiva and Tenon's capsule from the upper border of the medial rectus temporally about the globe concentric with and five mm. posterior to the limbus, to the inferior border of the medial rectus, excepting the areas over the insertions of the vertical recti. The lateral rectus is sutured and severed from the globe. The inferior oblique is cut close to the sclera. The two nasal arms of the graft are passed forward from the posterior aspect of the adducted globe one each into the superior and inferior nasal quadrants. By the same process, the temporal arms are passed forward into the anterior temporal quadrants and all four arms gently tightened. The ends are then sutured into predissected lamellar scleral grooves. 5-0 white braided silk was used for this purpose. The lateral rectus is resutured to its insertion and conjunctiva; Tenon's capsule is closed with running plain catgut sutures. The canthotomy is closed with one or two interrupted sutures, and one intermarginal lid suture inserted to prevent corneal trauma during the reaction from anesthesia.

Employing this technique, two series of experiments were conducted. In the first series, autologous material was used, seven operations each of fascia lata and Achilles tendon, for a total of 14 experiments. These animals were killed postoperatively at periods of from three to 16 months.

Results

Autologous donor series

Antemortem. There were no defects noted in these eyes other than one superficial corneal scar secondary to postoperative abra-

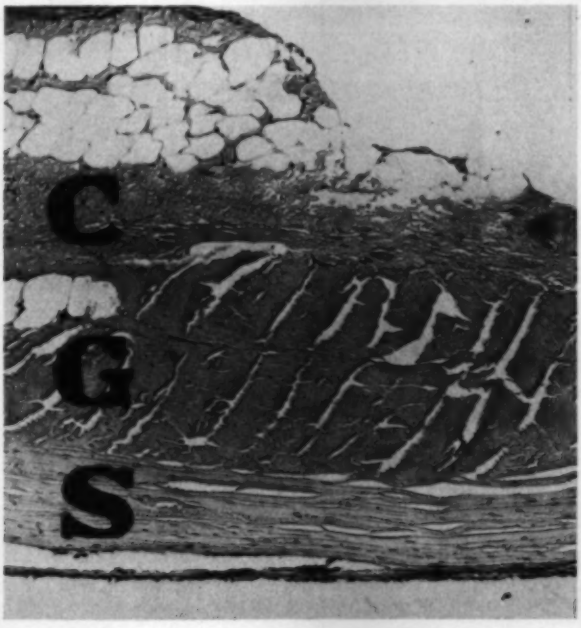

Fig. 1 (Curtin). Autologous tendon graft. Sclera (S) is in excellent coaptation with tendon graft (G) which demonstrates a well-developed connective tissue capsule (C). (Hematoxylin-eosin, ×100.)

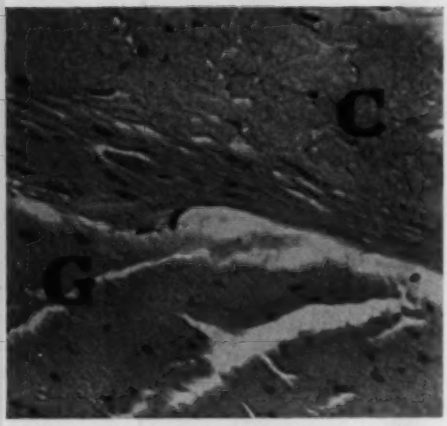

Fig. 2 (Curtin). Autologous tendon graft. Higher magnification, showing normal morphology of graft (G) and its vascular capsule (C). (Hematoxylin-eosin, ×284.)

sion. Corneal sensitivity, pupillary reactions, tonometric tension and fundus studies were all normal.

Postmortem. Macroscopically, all grafts took well and were in excellent position on the globe. There did not appear to be any atrophy or reabsorption. A well-developed envelope of connective tissue was consistently seen covering the graft and binding it to the sclera. In two specimens, both fascia, the graft was loose at the posterior pole. In both these instances, muscle (inferior oblique) was present between graft and sclera. Here the surrounding envelope of connective tissue was diminished or absent and the graft, due to its laxness, was mechanically incapable of reinforcement.

Occasional specimens were subjected to direct posterior traction on the graft after its dissection off the posterior pole. Of three eyes, the average fascia graft withstood 3.0 kg. of traction while three tendon grafts averaged 4.3 kg.

Microscopic examination of the globes demonstrated normal findings. All grafts displayed normal collagen staining characteristics and the fibrocytes were normal in morphology and number. The generous surrounding connective tissue previously noted about the graft was clearly demonstrable in all specimens (fig. 1 and 2) but this was seen to be diminished or absent where the graft was not in contact with the sclera (fig. 3). This mantle of tissue was rich in blood vessels and reticular fibers. No cellular in-

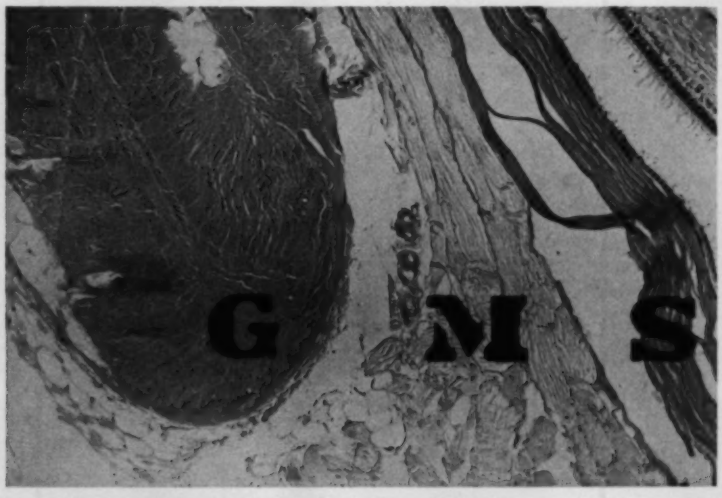

Fig. 3 (Curtin). Autologous fascia graft. Interposed muscle (M) is present between sclera (S) and graft (G). Note poorly developed capsule. (Van Gieson, ×100.)

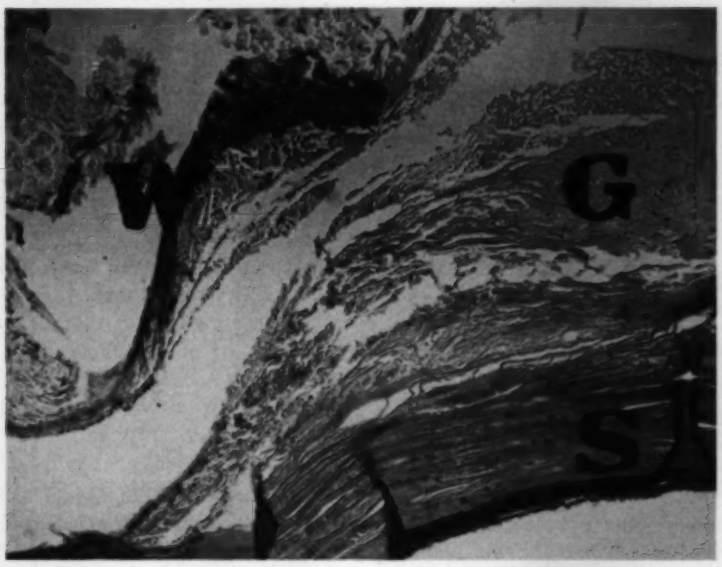

Fig. 4 (Curtin). Autologous fascia graft: Illustrates the absorption, vascularization and cellular invasion of graft (G) at insertion into anterior sclera (S) in proximity with silk suture (W). (Acid mucopolysaccharide stain, ×100.)

vasion or vascularization was seen in any instances other than at the graft insertions in the immediate presence of silk sutures. Here a foreign-body reaction to the suture was seen with accompanying cellular invasion and vascularization of the graft (fig. 4). In all other respects, the globes displayed normal anatomic findings other than the one aforementioned instance of corneal scarring.

Homologous fascia lata, Achilles tendon and sclera were then used as donor material in a second series of nine operations, three of each type graft. The follow-up periods varied from four to 10 months.

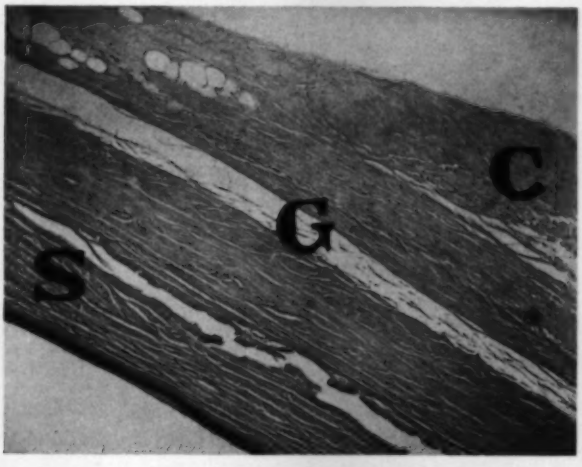

Fig. 5 (Curtin). Homologous fascia graft. Sclera (S) and graft (G) are in excellent contact. Graft capsule (C) is well developed. Due to fixation there are lamella separations in both the sclera and graft. (Van Gieson, ×82.)

Fig. 6 (Curtin). Homologous fascia graft. High magnification of Figure 4, showing the graft (G) with its connective tissue envelope (C). (Van Gieson, ×195.)

HOMOLOGOUS DONOR SERIES

Antemortem. One eye developed granuloma at one of the insertions of the graft due to a dehiscence of the conjunctival incision. The examinations, including corneal sensitivity, pupillary reactions, tension by tonometer, and ophthalmoscopic studies, were otherwise normal.

Postmortem. Macroscopically, all grafts were well positioned. Three grafts, one of each type, had muscle interposed between sclera and graft at the posterior pole and in these instances the grafts were loose. The grafts otherwise were tightly bound down onto the sclera by connective tissue and could be separated from it only with considerable difficulty. Some grafts appeared to have lost some substance but the extent of this process could not be accurately determined. Traction tests indicated tendon to be again stronger than fascia, the former withstanding 3.5 kg. while fascia was capable of withstanding 2.0 kg.

Microscopic. Normal cytology and staining properties were demonstrable in all grafts. The mantle of connective tissue

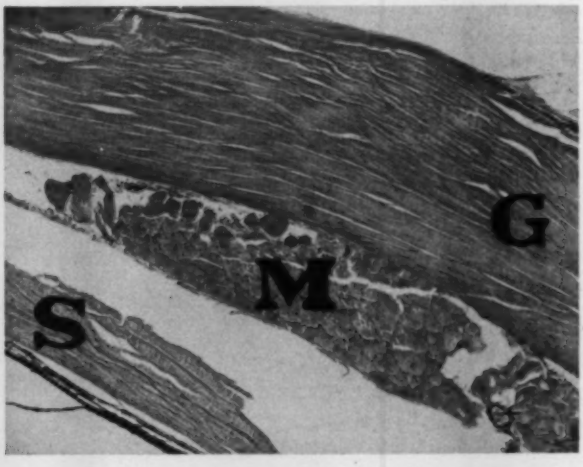

Fig. 7 (Curtin). Homologous tendon graft. Interposed muscle (M) between sclera (S) and graft (G) illustrating the absence of connective tissue capsule about graft. (Hematoxylin-eosin, ×70.)

about the graft could again be seen (fig. 5 and 6), although again they were absent in areas where scleral contact was lacking (fig. 7).

In scattered areas, notably those with poor scleral contact and absent connective tissue capsules, the surface of the graft was vascularized and there was some tissue resorption (fig. 8).

Some specimens strikingly illustrated the firm adhesion of graft to sclera. In one instance the sclera actually split with its outer layers adherent to the graft (fig. 9). Another point of interest was that several eyes had patent blood vessels and normal nerves interposed between graft and sclera (fig. 10). The graft did not appear to interfere with their function. Silk sutures produced identical effects upon the insertions of the homologous tissues as previously noted upon autologous grafts. Other than the granuloma noted during the macroscopic studies, the eyes were normal in all histologic details.

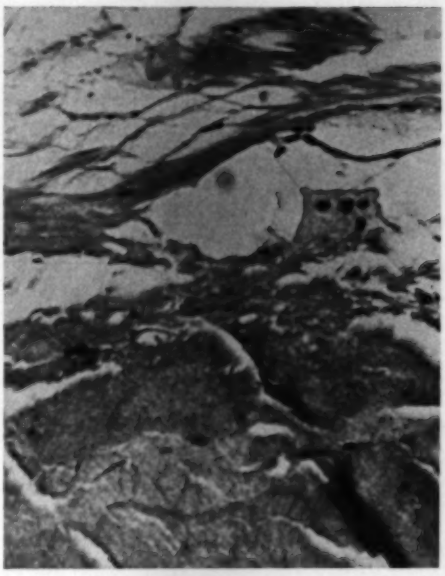

Fig. 8 (Curtin). Homologous scleral graft. Absorption of periphery of graft with destruction of collagen lamellae, vascularization and round cell invasion (Van Gieson, ×195.)

Discussion

The results of this study indicate that the principle of using a periscleral sling appears physiologically valid with the postulated prerequisites for the operative procedure fully satisfied. The periscleral cruciform graft uses normal anterior sclera as its base and with its intersection at the center of a weakened area can effect support from four directions. Scleral arc contact would seem to be of primary importance to the procedure.

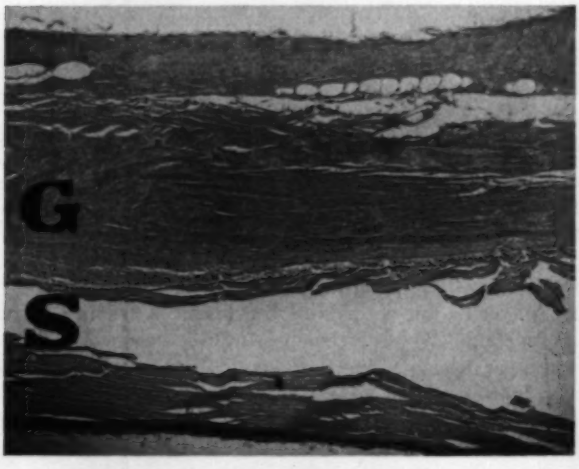

Fig. 9 (Curtin). Homologous fascia graft. Sclera (S) has split with its outer layers remaining adherent to the graft (G). (Van Gieson, ×100.)

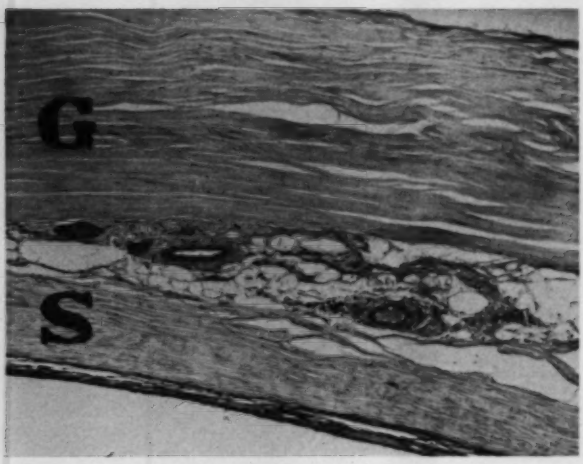

Fig. 10 (Curtin). Homologous tendon graft. Patent posterior ciliary arteries with nerves demonstrating normal details present between graft (G) and sclera (S). (Verhoeff, ×82.)

This is not only true for the actual ability to render mechanical support but also for the development of the mantle of surrounding connective tissue and possibly the ultimate health of the graft.

The connective tissue mantle can be found spreading from one arm of the graft to another where they are in proximity at the posterior pole. This effect gives an additional area of support at the intersection of the graft.

The usual snugness of the graft, even in instances when it was applied loosely, suggests some normal postoperative shrinkage. This has been noted in other related studies.[15,16] It is possible that interposed muscle in some way inhibits this reaction.

The operation is relatively harmless. In spite of deliberate attempts to produce complications by the rough handling of tissues, severance of vortex veins, suturing the graft very snugly to the globe, and the like, the only problems encountered were an unrelated corneal abrasion and conjunctival granuloma. It is of special note that the blood vessels and nerves present between graft and sclera retained their function much as they would in their intrascleral course.

The procedure is sufficiently versatile so that different areas of sclera can be reinforced with only minor changes in technique.

In regard to the material used, it should be noted that chemical agents calculated to produce tracts of periscleral fibrosis met with singular failure. Oddly, the best material for producing such fibrosis appears to be collagen itself.

Dense collagen, autologous or homologous, is compatible with both globe and orbit. It unites well with sclera not only at its insertions but there is added evidence that a certain amount of such union takes place along the entire extent of the graft.

From general work in the field, it is usually held that autologous tissue is superior to homologous as donor material.[17] These experiments do not yield any conclusive findings along these lines. All grafts took well. As a group, the homologous grafts appeared to be thinner but there were no striking histologic differences between the two types. The autologous tissues demonstrated superior tensile strength but the series of experiments is not sufficiently large to permit a definite conclusion. Certainly, both types give support well in excess of physiologic limits of stress. Tendon grafts gave better values than fascia in traction tests. This may have to do with its longitudinal bundle pattern in distinction to the layered

pattern of fascia which is only predominantly longitudinal. In general, the donor tendon used was decidedly thicker than fascia and this alone could account for the discrepancy. Another factor which may affect the strength of the graft is the suturing. Retained silk sutures produce a foreign-body reaction, with vascularization and cellular infiltration at the grafts insertions, and this could greatly diminish its strength. In the testing of graft strength, however, most grafts ruptured at the posterior pole not at their insertions. The malleability of the donor material is of great importance and, in this regard, fascia was superior to either tendon or sclera. Here again, the thickness of the donor material was a great factor.

It must be emphasized that this study has dealt exclusively with normal animal donor tissue and normal animal eyes. In the extrapolation of this work into clinical use for scleral reinforcement to arrest cases of progressive sclerectatic myopia, several theoretic problems arise beyond the actual mechanics of the surgery. There is, for example, the possibility that the disease process affecting the sclera will also involve the contiguous graft. This has recently proven to be the case in the use of fascia grafts to repair scleral defects due to scleromalacia perforans.[18] The invasion of the graft by abnormal host fibrocytes which would elaborate an abnormal ground substance into the graft itself could greatly affect this tissue's strength. There is also the possible action of injurious metabolites, such as enzymes and hormones, upon the graft, which could fully involve normal donor tissue in the disease process. In the matter of autologous donor tissue, there is the added question of associated connective-tissue defects in the organism which would interdict the use of such fascia and tendon grafts.[19,20] These questions can only be answered after extensive clinical trial.

Conclusion

This series of animal experiments has indicated that periscleral collagen grafts, both autologous and homologous, are well tolerated by the globe, are relatively harmless and are capable of effecting support of the posterior sclera in a range beyond physiologic stress. These results warrant a clinical trial of the procedure in progressive sclerectatic myopia.

2488 Grand Concourse (58).

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A COMPARISON OF MIOTICS IN ACCOMMODATIVE ESOTROPIA*

JAMES E. MILLER, M.D.
Saint Louis, Missouri

In the past 10 years renewed interest has been shown in the use of miotics for accommodative esotropia. The agents used prior to this were usually cholinergic drugs such as pilocarpine.[1] These, however, were found to be inconsistent in their effect and required frequent administration. More recent reports[2-4] have described the use of isoflurophate (DFP, Floropryl) which is a potent cholinesterase inhibitor. This miotic has a prolonged influence on accommodative esotropia.

The main disadvantage with isoflurophate has been instability in the presence of water. For this reason anhydrous oily bases not readily available were required. In the event that contamination with moisture occurred, there was a marked decrease in potency and, consequently, a diminished clinical effect. Several side-effects have been noted, such as iris cysts, headaches, and sensitivity to the medication or its base. The most common complication has been iris cysts, with an incidence of about 50 percent.

Isoflurophate appeared more effective in patients with accommodative esotropia and moderate hyperopia (less than +3.0D.). The greatest response was noted in patients with an esotropia more marked for near, namely, the convergence excess type. Often miotics were combined with the distance refractive correction to decrease the remaining esotropia for near. The withdrawal of glasses could also be accomplished more quickly with these medications, and eventually the miotic itself gradually eliminated.

Recently water-soluble inhibitors of cholinesterase have become available for use in glaucoma. These drugs are echothiophate (Phospholine) iodide, demecarium bromide (Humorsol or BC-48), and Mintacol.

Echothiophate (Phospholine) iodide[5,6] is a quaternary form of thiophosphate anticholinesterase compound which has a miotic effect from seven to 27 days. The usual glaucoma concentration is 0.25 percent. An aqueous solution of this compound has been described as stable indefinitely under refrigeration.

Demecarium bromide[7,8] (Humorsol, BC-48) or decamethylene bis-(m-dimethylaminophenyl N-methyl-carbamate) dimethobromide) is also a quaternary ammonium compound which produces miosis for as long as 10 days. Refrigeration is not required to maintain activity. A solution of 0.25 to 1.0 percent is used in glaucoma.

Mintacol[9,10] (diethyl-phosphoric-acid-p-

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nitrophenol ester) is manufactured in Germany by Bayer and has properties similar to eserine. A 0.01 to 0.02 percent solution will produce miosis for over 24 hours. There is no problem with stability, but the duration of action is much shorter than the others.

Since all of these compounds will soon be available at local pharmacies, it was thought that a clinical comparison of these drugs and isoflurophate would be useful. In addition, it was possible to vary the concentration as well as the frequency of administration.

I. Method

A. Dosage

Initially a small group of patients with accommodative esotropia who were well controlled on 0.025-percent isoflurophate were used to determine adequate concentration and frequency of administration. These patients had been binocular without glasses and had an esophoria of less than 10 diopters while using the ointment every other day.

It was found that echothiophate iodide in concentration of 0.1 percent every other day gave comparable results. Similar findings were obtained with 0.25-percent demecarium bromide. It was necessary to use 0.015-percent Mintacol twice a day to duplicate the isoflurophate results. More dilute miotics produced either a diminished or no effect, and with less frequent dosage there was a decline in response between applications.

B. Comparison of results

Miotics have been shown to alter the accommodative convergence ratio so that less convergence is produced by the same amount of accommodation. Consequently, the effect of miotics is most obvious in hyperopia and while accommodating for near. In addition, it also has been observed that fusional ability is increased with prolonged administration of isoflurophate.[11] This gradually appears without further evidence of changes in the accommodative convergence ratio.

In view of these observations, it was decided to evaluate patients in the following manner: Distance and near measurements were obtained on accommodative targets with and without the full cycloplegic refraction by the prism and alternate cover test. The distance correction was reduced by three diopters and the amount of convergence induced by this measured. Accommodative convergence was determined in this manner.

In order to eliminate proximal and tonic convergence, a three-diopter plus correction was placed over the refraction and the near measurement at one third of a meter repeated. The remaining esotropia or phoria was assumed to represent tonic and proximal convergence. The difference between the two near measurements was the convergence produced by the additional accommodation for near.

The improvement in fusional ability was also evaluated by measuring the amount of concave lens needed to change the patient from no deviation to an esotropia for both distance and near. In older children it was also possible to measure relative fusional divergence by the use of the Troposcope.

All cases were examined with a slitlamp for iris cysts. The parents and subjects were also questioned about side-effects and the actual frequency of medication.

In order to compare the relative effect of each miotic, the patients were changed to a different medication at intervals of two weeks to a month.

For the purpose of this study, a five prism diopter improvement in esotropia between miotics was considered significant, and this could be present for either distance or near. Pertinent fusional change was defined as six prism diopters change in fusional divergence, or one diopter of minus in the amount of concave lens required to produce an esotropia.

II. Results

In 38 patients, it was possible to compare results for isoflurophate, demecarium bro-

mide and ecothiophate iodide. In 15 of this group Mintacol was also used. Only a small quantity of this miotic was available which limited its application. The ages ranged between four and 13 years, and the refractive errors (spherical equivalent) were between +0.75D. to +7.5D. Fifty-five percent (21) were between +3.0D. to +5.0D. Twenty-four percent (9) below, and 21 percent (8) above. Vision was 20/40 or better in each eye under therapy.

The results are tabulated in Table 1. The comparison was made between isoflurophate and the various miotics. All patients improved on therapy and in only 10 instances was there a difference in the accommodative effect of miotics. Those patients who had an accommodative convergence decrease of five prism diopters or greater are listed. Similarly, a relative fusional divergence increase of over —1.0D. and/or six prism diopters of divergence amplitude was present in 12 individuals. These are also tabulated.

In the 10 instances where there was a difference of over five prism diopters in convergence, echothiophate iodide and isoflurophate each produced a greater effect in four. With demecarium bromide no improvement was noted, while two of the 15 using Mintacol showed a decrease. None of the miotics appeared to be superior in decreasing accommodative convergence.

Even the small increment of five prism diopters of fusional divergence or an additional diopter of accommodation failed to show any superiority in the various miotics (table 1). In 12 patients an alteration of relative fusional divergence was noted. Isoflurophate produced slightly better response in four patients; echothiophate iodide in five; demecarium bromide in one; and Mintacol in two.

From the standpoint of management it would be desirable to know the rapidity of action of the various miotics. In order to demonstrate this, four patients with accommodative esotropia were given an initial dose of isoflurophate and evaluated over a four-hour period. Continued improvement was observed over this time. These individuals were then rechecked in one week and further improvement was noted. No further change in measurements had occurred at the end of one month.

Similar results were obtained in eight other individuals using echothiophate iodide and Mintacol. Demecarium bromide appeared to have a faster rate of action in four patients since almost maximum effect was observed in two to three hours. There was a small decrease in esophoria noted at the end of a week.

The refractive change was also observed during the reported time-study. Less than 0.5 diopters of induced accommodation was recorded in all instances. This was determined by manifestly refracting the patient during the four-hour observation and upon his return.

Intolerance to medication was more striking in older children and adolescents. The majority of patients over the age of 13 years refused to use any of the miotics because of intense headache and eyeache. Even the appearance-conscious girls preferred glasses to miotics.

TABLE 1

COMPARISON OF NEWER MIOTICS AND ISOFLUROPHATE

Drug	Patients	Convergence Decrease	Relative Fusional Divergence Increase
Isoflurophate	38	4	4
Echothiophate iodide	38	4	5
Demecarium bromide	38		1
Mintacol	15	2	2
TOTAL		10	12

TABLE 2

SIDE-EFFECTS

Drug	Patients	Cysts	Headache	Keratitis
Isoflurophate	35	19 (54%)	3 (8%)	2
Echothiophate iodide	51	12 (23%)	2 (4%)	0
Demecarium bromide	24	5 (21%)	0	0
Mintacol	16	7 (44%)	2 (12%)	0

It was also noted in the patients used for the comparative study that iris cysts usually developed within the first month in susceptible patients, and persisted even when the miotic was changed. This prevented an accurate comparison of the incidence of cysts. A larger group of patients (116) who had been maintained on one type of miotic were evaluated for the incidence of cysts and other complications. These are listed in Table 2.

The greatest incidence of cysts was found using isoflurophate. This was present in 19 out of 35 patients (54 percent). Mintacol gave the second highest percentage with seven out of 16 patients (44 percent). Echothiophate iodide and demecarium bromide were about comparable, with echothiophate iodide producing 12 instances in 51 individuals (23 percent) and demecarium bromide five in 24 (21 percent). The cysts generally appeared in two to six weeks with all of the medications used. The majority of patients were continued on the miotics in spite of the cysts, with no untoward effects.

There were five individuals who developed headaches following miotic therapy. This occurred in three patients (eight percent) using isoflurophate and in two (four percent) on echothiophate iodide. This side-effect occurred shortly after the first installation of the miotic and gradually disappeared over a two-month interval. The two instances of keratitis listed with isoflurophate were of the superficial punctate variety, with the majority of the infiltrates located just distal to the limbus. These lesions disappeared on the cessation of isoflurophate.

Another observation was the variability in pupil size in patients who had an obvious clinical effect from the miotics. The variability was most striking with echothiophate iodide and demecarium bromide. In some patients the pupils were of normal size and responded in the usual fashion to both accommodation and light. Generally these patients did not have iris cysts. Others had moderate to marked constriction of the pupil with very little pupillary response. Isoflurophate and Mintacol usually produced an intense persistent miosis in which no pupillary constriction could be elicited.

Tolerance to miotics appeared in several of the subjects with prolonged use. These patients often showed the initial improvement when the miotic was changed. This is comparable to the resistance seen in glaucoma patients and the improvement upon changing their medication.

All of the newer miotics were tried in postoperative patients in which there was a remaining esotropia. There were no undesirable effects observed from using these medications as soon as the second postoperative day. A definite decrease in the esotropia was noted upon several occasions.

III. Discussion

From these results it would appear that the water-soluble cholinesterase inhibitors produce a similar clinical effect to isoflurophate. They do not appear superior to the latter, but do offer certain advantages, namely, ease of dispensing and greater stability. All of the water-soluble compounds appeared stable over a two-month interval. After this period there appeared some decline in the effect of echothiophate iodide, even when it was refrigerated. On the other

hand, echothiophate iodide produced a slight improvement in accommodative esotropia when the patient had been on demecarium bromide.

The incidence of side-effects, particularly iris cysts, was reduced using echothiophate iodide or demecarium bromide. Isoflurophate would often elicit large abundant cysts, whereas those produced by echothiophate iodide and demecarium bromide were of a small variety and not as abundant. It did not seem possible to alter iris cysts once they had occurred by changing the miotic. In two instances isoflurophate was discontinued and the cysts allowed to disappear; then echothiophate iodide was used without developing cysts.

The development of tolerance to miotics was very similar to that seen in glaucoma. Some patients gradually increased their esotropia with prolonged therapy. However, after changing to another miotic, they would then demonstrate the initial response. It was also possible to reinstitute the miotic and control the strabismus after stopping the medication for a period of time.

The water solubility from an esthetic standpoint is much desired by patients and parents, and there appeared less reluctance to using these medications. There was also no alteration of wound healing following muscle surgery with the use of these compounds. Previously there was hesitance in using an ointment for this reason.

It did not appear feasible to determine the maximum response of a patient to a miotic by observing him during a four-hour interval. Alteration in his accommodative convergence ratio occurred for a longer period. Evaluating a patient over two hours in an office gives some indication, but the maximum effect appears later.

Another side-light in this investigation was the potentiation of bifocals by the use of miotics. It was often possible to eliminate a small residual esotropia remaining through the bifocals with miotics. With the gradual development of fusional amplitudes, miotics or bifocals could be eliminated.

The aqueous miotics were an excellent adjunct in removing glasses from patients with accommodative esotropia. After maintaining these patients on full-strength miotics, the concentration could be reduced. This produced a decrease in the effect of the miotics, but this diminution was of a uniform nature. A reduction in periodicity of application tended to give an uneven response.

IV. Summary and Conclusions

1. Water-soluble cholinesterase inhibitors such as echothiophate iodide, demecarium bromide, and Mintacol, are comparable to isoflurophate in the therapy of accommodative esotropia.

2. Side-effects are reduced with these newer miotics.

3. Water solubility gives greater flexibility in administration.

4. Tolerance develops to miotics in accommodative esotropia.

640 South Kingshighway (10).

Drugs were supplied through the courtesy of the following: Echothiophate iodide (Campbell Pharmaceuticals, Inc., 254 West 31st Street, New York 1, New York); Isoflurophate and demecarium bromide (Merck Sharp & Dohme Research Laboratories, West Point, Pennsylvania); Mintacol (Bayer, Leverkusen, Germany).

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STEROID TREATMENT OF HERPES-SIMPLEX INFECTIONS OF THE CORNEA*

GEORGIA A. MCCOY, B.A., AND IRVING H. LEOPOLD, M.D.
Philadelphia, Pennsylvania

Three new analogues of hydrocortisone, Kenacort (triamcinolone), Medrol (6-alpha methyl delta[1] hydrocortisone), and Decadron (dexamethasone or 9-alphafluoro 16-alpha methylprednisolone), have recently become commercially available. An attempt to evaluate their therapeutic effect on herpes simplex infections of the cornea has been made because earlier steroids have been shown to aggravate herpes simplex keratitis in the experimental animal and human eye.[1-5]

EXPERIMENTAL DATA

Thirty-four corneas were de-epithelized by lightly rubbing the side of a 21-gauge needle over the surface of the cornea. From a 27-gauge needle, one drop of a saline solution containing approximately one million pocks of Herpes simplex was placed on the abraded cornea. Thirty-six hours later treatment consisting of two drops of one-percent steroid three times a day was begun. Daily treatment was continued until all eyes were free from lesions. Three groups of four rabbits each were treated with Kenacort, (Squibb), Medrol (Upjohn), and Decadron (Merck, Sharp and Dohme), respectively. Five other rabbits served as controls. Examinations were made every 48 hours after staining the lesions with methylene blue. Drawings of all eyes were made on the third, fifth, seventh, and 10th days (fig. 1).

RESULTS

Figure 1 diagrammatically compares the extent of herpetic lesions in all eyes.

On the third day after infection, characteristic dendritic ulcers were present on all of the rabbit corneas.

By the 10th day, five out of 10 of the control eyes were lesion free. Three of the remaining five eyes appeared normal by the 12th day, and the others were clear by the 13th day after infection.

At the same time, four of the Kenacort-treated eyes showed signs of slight improvement. By the 12th day three eyes were clear as were the remaining ones by the 17th day after infection.

The herpetic lesions treated with Medrol lasted 14 to 24 days, while those treated with Decadron were still present 17 to 25 days after herpes injection. Seven dendritic ulcers treated with these two latter drugs (three

* From the Research Department of the Wills Eye Hospital.

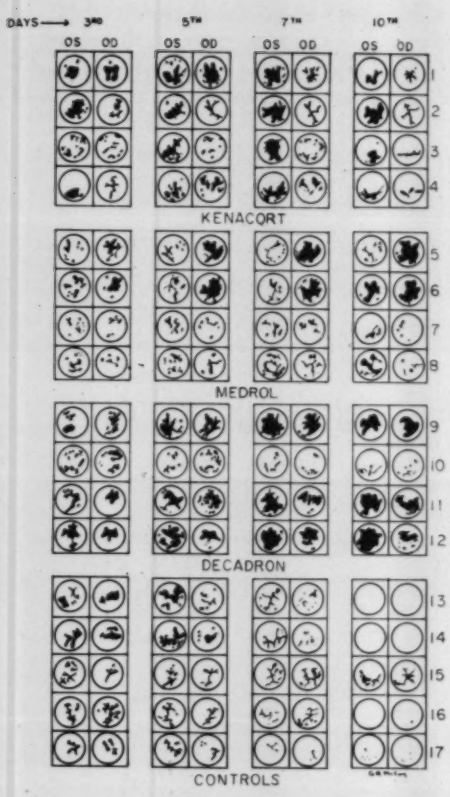

Fig. 1 (McCoy and Leopold). Dendritic ulcers produced by the application of one drop of a saline solution containing approximately one million pocks of Herpes simplex on abraded corneas.

with Medrol and four with Decadron) appeared to have increased in severity after the seventh day of treatment.

Summary

1. Thrice daily treatment with two drops of one-percent Kenacort (triamcinolone), Medrol (6α methyl Δ^1hydrocortisone) and Decadron (dexamethasone) appears to prolong the time required for herpes simplex infections of the rabbit cornea to heal. Kenacort-treated lesions lasted two to three days longer; Medrol-treated lesions lasted four to 10 days longer; and those lesions treated with Decadron lasted seven to 11 days longer than did the lesions of those eyes which received no treatment at all.

2. Medrol Decadron seem to continue to increase the severity of some lesions after seven days of treatment.

1601 Spring Garden Street (30).

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BLEPHAROPHIMOSIS AND ITS OPERATION*

LAJOS NÉMETH, M.D.
Budapest, Hungary

Ophthalmic literature offers only few and somewhat confused data about the origin, essence, and types of blepharophimosis, a rare disease. Moreover, some publications described shortening of the palpebral fissure by ankyloblepharon as blepharophimosis. Though it is incorrect to use the terms, epicanthus and blepharophimosis, to denote the same condition, one often encounters this false usage. The term, epicanthus, refers to the plica verticalis which most frequently covers the inner but seldom the outer canthus and which extends itself curtainlike over the angle.

The various forms have been clearly classified by Spaeth who distinguishes epicanthus supraciliaris, palpebralis, tarsalis and inversus. These names indicate the originating areas of the plica which covers the angle. Accordingly different operative procedures may be used to correct this deformity. The epicanthus is frequently a familial disease often associated with other hereditary disorders. These disorders must be sharply differentiated from the real blepharophimosis, that is, the horizontal shortening of the palpebral fissure and its deformation.

The most apt grouping is by Duke-Elder who speaks about senile, spastic, and cicatricial blepharophimosis. As these terms imply, the first group is caused by senile atrophy of the tissues, the second by spasm of the orbicular muscle, the third by some cicatrization. The length of the palpebral fissure may be changed as a result of one of these causes.

Velhagen adds two forms of blepharophimosis to the list: blepharo chalatica and ptotica. Both names indicate the nature of the trouble. According to Velhagen the etiology is not clear, disturbances of endocrine origin may play a part. Of all these forms of blepharophimosis, the senile form has the greatest importance but even this form is so rare that few ophthalmologists, even those with extensive practices, can boast of ever having observed a case.

Books on eye surgery seldom describe the operative technique for this type of deformity. Elschnig has proposed a solution for the dislocated external canthus. He took a six-mm. periosteum flap from the external orbital edge, directed it backward and fixed it horizontally. He sutured this flap with one stitch to the upper and another to the lower external edge of the tarsus, working it under the skin of the external canthus.

This periosteum flap was designed to replace the unelastic and atrophied external ligament of the canthus. Even while publishing this procedure, Elschnig conceived a modification, which he proposed to carry out if he were ever to operate a similar case. For repairing abnormalities of the external canthus Spaeth's book on surgery contains a suggestion by Wheeler. Wheeler prepared a four mm. band of orbicularis muscle near the external canthus adjacent to the upper and lower eyelids and, crossing these, he sutured them to the periosteum of the orbital edge. He closed the skin incision with fine stitches (fig. 1).

In both procedures the result depends on one factor. The weak nourishment of the periosteum flap and the weak adhesion of the crossed muscle bands to the orbital edge or the subsequent loss of their elasticity are sufficient to diminish the result. Therefore, it seems advisable to devise an operation which would secure the stability of the position of the external canthus. I was fortunate in being able to observe a patient suffering from senile blepharophimosis and could plan the necessary operation.

After successful operation on both eyes, I

* From the Department of Ophthalmology, Hungarian State Railway Hospital.

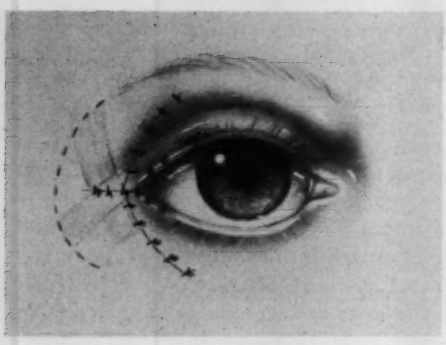

Fig. 1 (Németh). Wheeler's procedure.

achieved both excellent cosmetic and functional results.

Case report

H. Gy., a man, aged 58 years, declared that the skin of his eyelids had begun to sag 26 years before and from that time on the disfiguration of his eyelids slowly developed. He was operated for intestinal tumor by the surgical service and, after recovering from this, he was sent to our department for the treatment of his eyelids. Vision was: R.E., 5/5; L.E., with correction (myopic astigmatism), 5/15.

The width of the palpebral fissures was nine mm.; length 20 mm. Hertel test on both eyes 15/97. The external canthi were dislocated toward the nose to such an extent that the distance between the external commissure and the orbital edge had increased to double the normal. As a result of this, the external canthi overlay completely the temporal sclera and extended beyond the limbus, covering part of the external edge of the cornea. The external canthi were rounded, and the palpebral fissures had a characteristically changed form. The face was strikingly wrinkled, especially near the lower eyelids from where the wrinkles spread out fanwise. The insufficiency of the fat layer was also conspicuous (fig. 2).

Fig. 2 (Németh). Appearance of the patient.

Fig. 3 (Németh). Pulling back the loosened skin gave the patient a more normal appearance.

By gently pulling back the skin of the temporal area along the external edge of the orbit, the eyelids could be put into a normal position and the canthi regain their regular shape, the fissures their usual length, and the wrinkles, which ran from the skin of the lower lid, became less conspicuous (fig. 3).

According to Elschnig this alteration of the fissures is due to a senile loosening of the external canthus ligament, that is, of that of the fascia tarsorbitalis, the orbicularis muscle then dislocates the external canthus by drawing toward the inside. No significant alteration in the skin could be noted. Two methods suggested for shortening palpebral fissures are canthotomy and canthoplasty. In this case, however, neither could be applied successfully.

Operation

In the case here reported, it seemed advisable to achieve an extension of a plica to correct the deformity of the canthi and ensure normal papebral fissures. An oval excision of skin was made beyond the external orbital edge, the frontal curve of which ran almost to the edge of the orbit (fig. 4). Starting from the anterior excision line, the skin was folded back as far as the external canthus. Turning back the skin will reveal the tapered, atrophied, loose external canthus band. Near the external canthus a 3-0 catgut loop-stitch was placed in the external canthal ligament which was extended and sutured to the external periorbital edge (fig. 5).

Beyond the edge of the external orbit but not far from it, three sutures are stitched into the fascia temporalis. They are placed

Fig. 4 (Németh). An oval excision of skin was made beyond the external orbital edge, the frontal curve running almost to the edge of the orbit.

vertically under one another. These sutures shift the skin, which has been folded back to the external canthus, where they are tied and knotted over pearls (fig. 6).

Finally, the excision wounds are closed with fine knotted sutures. After the operation there will be a perpendicular wound line united by fine sutures beyond the external edge of the orbit. Some mm. in front of it and running parallel three sutures are knotted over pearls; these anchor the skin which was folded back to the external canthus at the beginning of the operation (fig. 7).

The sutures knotted over the pearls will have to be removed on the fifth or sixth day. One day after operation the area around the external canthus becomes a bit swollen but this subsides soon after the removal of the pearl sutures. Figure 8 shows the postoperative appearance.

Histologic examination of the excised skin

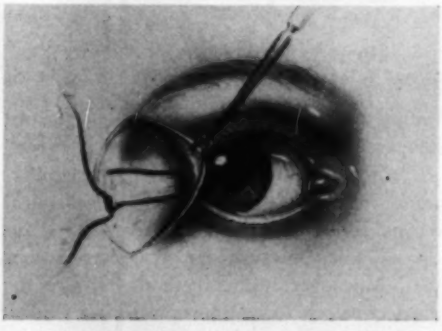

Fig. 5 (Németh). A 3-0 catgut suture was placed in the external canthal ligament which was extended and sutured to the external periorbital edge.

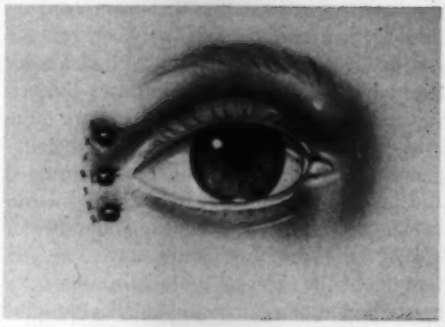

Fig. 6 (Németh). The sutures are tied and knotted over pearls.

Fig. 7 (Németh). Anchoring the folded-back skin to the external canthus.

Fig. 8 (Németh). The postoperative appearance of the patient.

shows it to be covered with several layers of thin regular epithelium. The fibers of the conjunctival tissue under the epithelium are tapered, somewhat disordered, and thinned in the lower strata. Here the fibers are quite fine. Elastic fiber stains show that the collagen fiber under the epithelium is disarranged and broken. The histologic picture gives an explanation for the looseness and extensibility of the skin. Looseness, extension, and atrophy of the external canthal ligament may be attributed to similar causes. Blepharophimosis is promoted by shrinking of the subcutaneous fat layer.

Comment

Blepharophimosis shows well-defined diagnostic characteristics. The condition must be distinguished from epicanthus. It can be cured by operation but the usual operative methods, canthotomy or canthoplasty, are not suitable. For repairing the senile form, the operation should insure a normal position of the external canthus and a normal form of the palpebral fissure. To do this three factors are necessary (1) the superfluous skin of the canthal area is removed by oval excision; (2) the slack external canthal ligament is tightened by fixing it to the periosteum of the orbital edge; (3) the skin of the external canthus is shifted temporally and, by fastening it with three sutures to the fascia temporalis, an adhesion is achieved which will prevent subsequent lengthening. The recommended operation has given perfect and complete cosmetic and functional results. This operation is easy to perform; no subsequent complications occur.

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STUDIES ON VITREOUS HYALURONATE*

Paper electrophoretic and chromatographic behavior of it and of its enzymatic break-down products

A. Kahán, M.D. and I. L. Kahán, Ph.D.
Szeged, Hungary

The properties of the vitreous gel are highly dependent on the state of its hyaluronic acid content which is known to be composed of fractions of different particle size even under normal conditions[5] as well as a variety of conditions in which its depolymerization occurs.[3,9] However (due to factors inherent in the methods employed), "free" electrophoresis and ultracentrifuge fractionation[18] of vitreous, liquefied by physical means, failed to furnish sufficient data about the polydispersity of its hyaluronate content. Moreover, these methods require too much vitreous to be appropriate for clinical and some experimental investigations.

The more economical procedures of paper

* From the Department of Ophthalmology, director: Prof. Dr. F. Kukán, and the I. Department of Medicine, Director: Prof. Dr. G. Hetényi, of the University Medical School.

electrophoresis (already employed in investigating protein fractions of human vitreous[19]) and of paper chromatography proved applicable to the separation of at least two mucopolysaccharide fractions from normal human, cattle, and guinea pig vitreous. Even better results were obtained from subretinal fluid aspirated at surgery for ablatio retinae (fig. 5) (this will be published separately).

The aim of the present paper is to investigate the cause of the different electrophoretic and chromatographic behavior of hyaluronate fractions and to correlate motility data of vitreous hyaluronate polymers with the grade of polymerization and chemical composition.

Materials and Methods

Undepolymerized vitreous hyaluronate was prepared from cattle eyes dissected equatorially one hour after death. The intact vitreous gels were collected in an ice-cooled glass cylinder, containing 5.0 ml. 0.5-percent sodium diaethyldithiocarbamate solution/100 ml. vitreous, to prevent nonenzymatic depolymerization. The structure was broken by straining the whole through cheese-cloth and filtering through glass filters G_3 and G_4. Adapting the method of Dorfman and Ott[6] to the vitreous body, as suggested by Alburn and Williams,[1] the filtrate was shaken with one-third volume of Hayem solution for one hour, and the protein precipitate centrifuged off completely. The supernatant was poured in three-volumes of ice-cold acetone, the stringy precipitate was collected by brief centrifugation and dissolved in 10-percent sodium acetate as little as possible, and shaken with one-fifth volume of chloroform amylalcohol (9 : 1) mixture, for 45 minutes. After centrifugation, the clear supernatant was syphoned off, precipitated with two-volumes ethanol at pH 5.0, collecting by brief centrifuging only the stringy precipitate, washed with ethanol and ether, and dried.

Solution of the dry material in saline proceeds slowly (24 hours) and incompletely, a clear solution being obtained by centrifuging. The concentration of hyaluronate may be determined by drying the residue at 100°C. until the weight is constant; this yields equivocal values, hyaluronic acid being very hygroscopic.

Instead of using this cumbersome method, the concentrations of the undepolymerized materials were generally estimated by the turbidity developed by adding to 0.1 ml. of its solution 0.9 ml. saline and 4.0 ml. of acidified serum protein prepared as described by Tolksdorf,[16] the extinction value of the turbidity being measured against blank with the Pulfrich photometer (d = 1 cm., S47 filter). More concentrated solutions give a stringy mucin clot with acidified serum protein, and turbidity can not be assessed adequately.

The acetyl glucosamine content was checked by the Morgan-Elson reaction as modified by Südhof and Schweer;[15] the glucuronic acid content by the carbazol reaction of Dische;[4] N determinations were performed by the Kjeldahl procedure.

Analytic data are: the solution was obtained by suspending 12 mg. of dry hyaluronate in 5.0 ml. saline and centrifuging; dry residue: 0.9 percent; extinction value (d = 1 cm., S47) of 0.1 ml. with 4.0 ml. acidified serum protein: 0.7; acetyl glucosamine: 160 mg. percent; glucuronic acid: 104 mg. percent; N: 23 mg. percent.

Gradual enzymatic depolymerization was performed by incubating at 37°C. 5.0 ml. vitreous hyaluronate solution (turbidity extinction value: 1,2) adding 10 VRU bacterial hyaluronidase (Hyason, Organon) dissolved in 0.1 ml. saline. At intervals, 0.1 ml. of the reaction mixture was withdrawn and the turbidity values checked; they were falling with progressive depolymerization. (The data of a representative experiment are given in table 1.) Having reached characteristic turbidity values, each time 0.4 ml. of material was withdrawn, the enzymatic activity was stopped by immersing the sample in a boiling water bath for 60 seconds, freezing immediately, and storing in the frozen state.

Enzymatically fully depolymerized hyalu-

TABLE 1

TURBIDITY VALUES OF THE REACTION MIXTURE OF FIVE ML. VITREOUS HYALURONATE PLUS TEN VRU HYASON, INCUBATED AT 37°C.

Samples Stabilized	Before adding Hyason	After Incubation of Mixture for Minutes					
		5	35	60	70	80	95
Turbidity developed on addition of 4.0 ml. acidified serum protein to 0.1 ml. reaction mixture diluted to 1.0 ml. with saline. ($E_{d-lem.,\ 547}$)	1.2 stringy	1.3	0.9	0.55 (not stringy turbidity)	0.32	0.14	0.08

ronate ("digest") was obtained by incubating at 37°C. for 24 hours a suspension of 50 mg. hyaluronate in 1.0 ml. saline containing 50 VRU Hyason. In some experiments this digest was further subjected to the action of liver β glucuronidase (Fluka), incubating 1.0 ml. of digest acidified with 0.05 ml. of concentrated acetic acid to pH 4.6 with 10 mg. of the enzyme, at 37°C. for 24 hours. After this period, it was neutralized with 0.125 ml. of 16-percent NaOH.

Paper electrophoresis was performed on horizontally stretched Whatman No. 1 filter-paper strips, with 6.2 v/cm. Undepolymerized and partially depolymerized materials were run 18 hours in veronal/acetate buffer, pH 8.6, of ionic strength:0,06. Samples (0.1 ml.) were spotted, melted just before use, near the cathode. Fully depolymerized materials (digests) and split products obtained through the action of glucuronidase were run in borate buffer solution, pH:8.6 (12 gm. boric acid, 10 gm. sodium borate in 1,000 ml. water), as sugars, hexuronic acids and hexosamines are known to form borate complex compounds in this environment and obtain characteristic motilities in the electric field.[2]

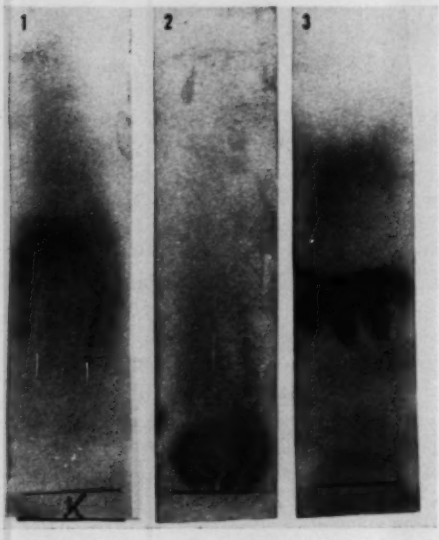

Fig. 1 (Kahán and Kahán). Paper electrophoresis strips (barbital buffer, pH 8.6) of (1) vitreous hyaluronate, (2) umbilical cord hyaluronate, (3) M. lysodeikticus wall mucopolysaccharide.

Paper chromatography was performed in an ascending direction for five hours at 37°C., spotting at a starting point 0.05 ml. of material on a Whatman No. 1 filter paper. Solvent: propanol/m/15 phosphate buffer, pH 6.5 (37:63), as described by Kerby[11] for the partition of different sulfated mucopolysaccharides. The chromatograms were air dried, immersed in ethanol, drained and dried, then twice drawn through three-percent acetic acid and drained, as described by Feeney and McEwen.[7] This procedure, besides fixing mucopolysaccharides, has the advantage of washing out phosphates which would interfere with the subsequent colloidal-iron staining procedure.

Papers with undegraded and not fully depolymerized materials were stained with the colloidal-iron staining procedure of Hale,[8] as modified by Rinehart and Abul Haj[14] for the detection of acid mucopolysaccharides in histologic sections, and adapted to filter paper by Feeney and McEwen[7] and modified by one of us.[10]

Reducing sugars and derivatives were visualized by the formazan reaction as described by Trevelyan, Procter and Harrison,[17] glucosamine by the Morgan-Elson reactions as adapted to filter paper by Partridge.[13] To investigate the chemical nature of the reducing spots, several paper strips spotted with the same digest were run simultaneously with known reference substances (dextrose, glucosamine and glucuronic acid). The papers spotted with the reference substances and one strip spotted with the digest were developed by the formazan reaction. The zones of the undeveloped paper strips corresponding to the location of the developed digest-streaks were cut to small pieces and extracted with 1.0 ml. warm (80°C.) borate buffer solution of the composition already given for 10 minutes, and the extract was separated from the paper pieces which were washed with an additional 0.5 ml. of the same buffer solution through a $12G_4$ glass filter by suction. The 1.0 ml. extracts were subjected to glucosamine and hexuronic acid determinations by the Morgan-Elson reaction as modified by Südhof and Schweer[15] (but hydrolysis for two hours with 2 N HCl), and by the carbazol reaction of Dische,[4] respectively.

Results

1. The electrophoretic behavior of unde-

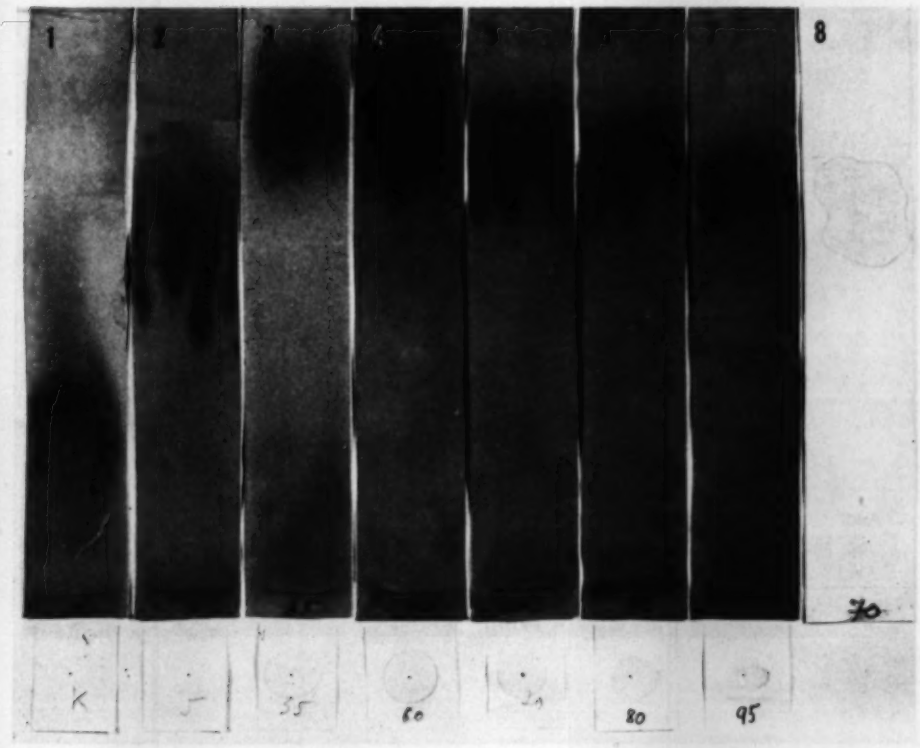

Fig. 2 (Kahán and Kahán). Paper electrophoresis strips (barbital buffer, pH 8.6) of enzymatic (hyaluronidase) depolymerization products of vitreous hyaluronate (see table 1). (1) Undepolymerized material. Stabilized at: (2) five, (3) 35, (4) 60, (5) 70, (6) 80, and (7) 95 minutes' incubation time, stained by the colloidal-iron procedure. (8) Product at 70-minute reaction time (formazan). (Below) 0.05-ml. spots of the materials named, stained by formazan reaction.

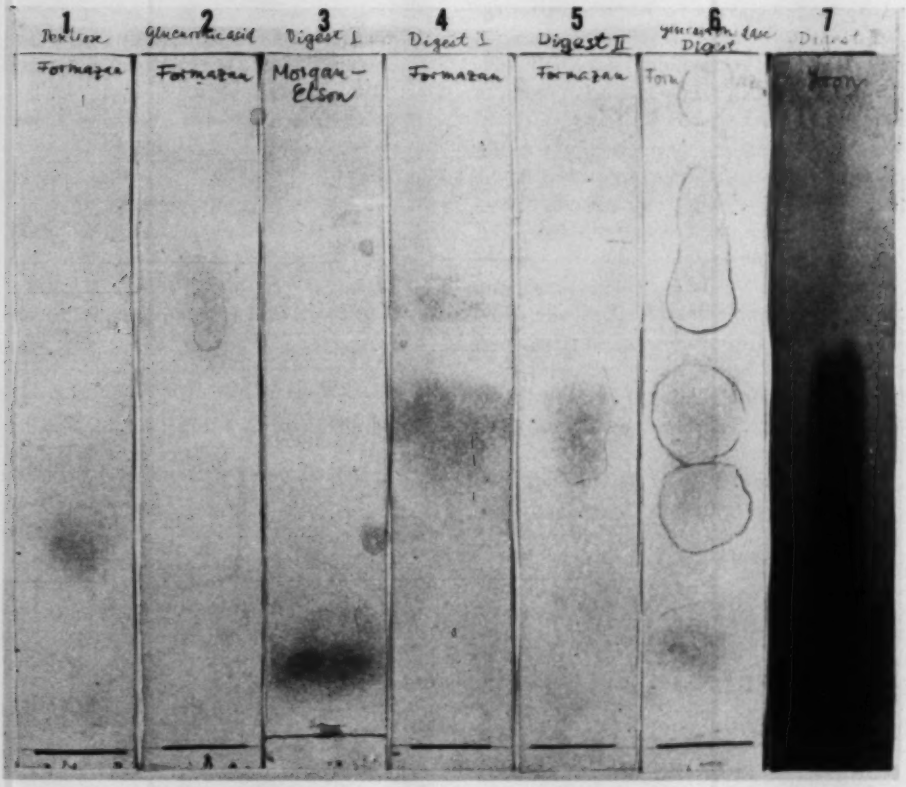

Fig. 3 (Kahán and Kahán). Borate electrophoresis strips of fully depolymerized vitreous hyaluronate digests and reference materials. (1) Dextrose. (2) Glucuronic acid. (3) and (4) Vitreous hyaluronate digested by hyaluronidase. (5) and (7) Hyaluronate digested to oligosaccharide and disaccharide units by hyaluronidase. (6) Oligosaccharide subjected to the action of glucuronidase. (3) was developed by the Morgan-Elson technique; (7) by the colloidal-iron. All others by the formazan procedure.

polymerized vitreous hyaluronate was compared with that of umbilical cord,[6] another example of nonsulfated acid hyaluronates, and with that of the neutral wall mucopolysaccharide of Micrococcus lysodeikticus prepared by the method of Meyer and Hahnel[12] (fig. 1). All three samples moved toward the anode in (pH 8.6) barbital buffer solution; vitreous hyaluronate moved four to five times faster than umbilical cord hyaluronate, both yielding practically a single streak, while the lysodeikticus mucopolysaccharide was separated to three components.

2. Gradual enzymatic breakdown (table 1) yields in the beginning different monodisperse depolymerization products, characterized by gradually increasing electrophoretic motility (in pH 8.6 barbital buffer solution) which has reached its maximal value when the turbidity has decreased to 80 percent of its initial value. Until this stage, no reducing substances were liberated. From this stage on, reducing substances are released at the expense of turbidity value but electrophoretic motility of the resulting polysaccharides and oligosaccharides of decreasing chain length is not further increased, and later it is even insignificantly decreased. By the formazan reaction, reducing substances are found at and behind the posterior border of

the partially depolymerized mucopolysaccharide fraction of maximal motility (fig. 2).

3. Borate electrophoresis of vitreous hyaluronate digests, fully depolymerized by the action of hyaluronidase, yielded three distinct boundaries.

The first could be visualized by the Morgan-Elson reaction as a violet band near the starting line, assumed to be acetyl-glucosamine.

The most intensive band was found at a distance 1.1 times longer from the starting line than that of the dextrose reference spot, when developed by the formazan reaction. The extracts of this zone proved to contain glucosamine and glucuronic acid in nearly equimolecular ratio, and is assumed to be a disaccharide consisting of these two compounds.

The third band was found to be faintly visualized by the formazan reaction and by its coincidence with the situation of the glucuronic acid reference spot, and, as its extract contained two times as much glucuronic acid as that of the disaccharide band, was assumed to consist of free glucuronic acid. However, the presence of this third band was often conjectural and sometimes missing. When the digest which failed to yield this third band was incubated with liver β glucuronidase, this third (glucuronic acid) band appeared with great intensity, and two additional bands were found by the formazan procedure, one behind the usual disaccharide

Fig. 4 (Kahán and Kahán). Paper chromatograms of vitreous hyaluronate depolymerization products by 25 VRU Hyason/ml. (1) Undegraded. (2) Product at zero minutes' reaction time. (3) At five minutes. (4) 20 minutes. (5) 30 minutes. (6) 50 minutes. (7) and (8) Fully depolymerized digests. Strips 1 to 7 stained by colloidal-iron. Strip 8 by the formazan procedure.

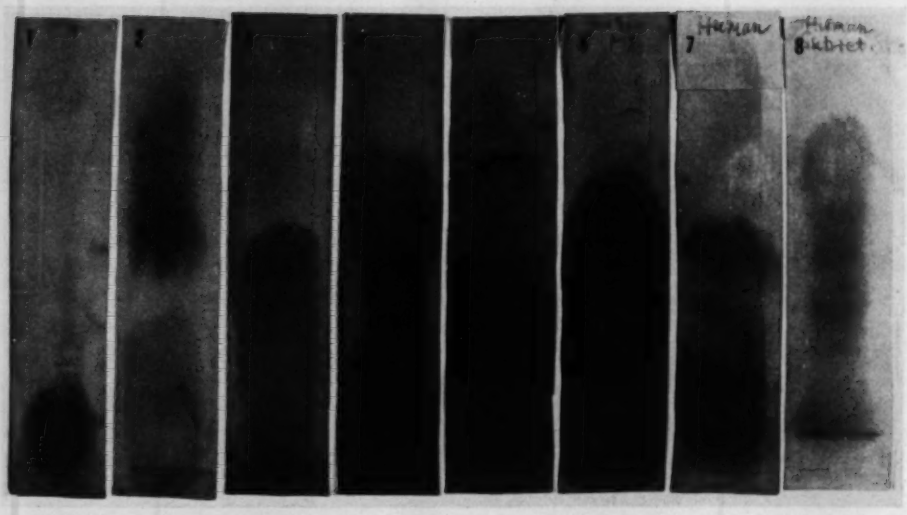

Fig. 5 (Kahán and Kahán). Paper electrophoresis strips (barbital buffer, pH 8.6) of (1) undegraded, (2) partially depolymerized, (3) totally depolymerized vitreous hyaluronate. (4) A mixture of 1+2+3. (5) Cattle. (6) Guinea pig. (7) Human vitreous filtrate. (8) Human subretinal fluid. Colloidal-iron stain.

band and one in front of the glucuronic acid band. Their nature, suspected to be other disacharides, is under investigation; they seem to be liberated from oligosaccharides (undetected by the formazan reaction but visualized by the colloidal-iron stain), just like free glucuronic acid from the disaccharide unit of the digest, by the action of β glucuronidase (fig. 3).

4. When subjected to paper chromatography by the method described, undegraded vitreous hyaluronate remained near the starting line, its depolymerization products exhibited increasing motility with decreasing chain length, as in the electrophoresis experiments; however, the motility was not maximal when reducing substances began to appear but, with progressing breakdown, the spots approached, and that of the fully depolymerized digest attained the solvent front, the front spot being visualized by the formazan procedure (fig. 4).

5. Mixtures of undegraded vitreous hyaluronate and of its depolymerization products of different chain length and of material completely digested by the action of hyaluronidase could be separated by paper electrophoresis in barbital buffer solution (pH 8.6) to a long semicontinuous band containing the fractions of different motility of the mixtures of which they were composed. The electrophoretic behavior of this mixture greatly resembled that of human, cattle, or guinea pig vitreous filtrate or that of human subretinal fluid withdrawn at surgery for ablatio retinae (fig. 5). Though bovine vitreous filtrate run in borate buffer solution proved to contain the usual disaccharide unit of hyaluronate digests (but only in scarcely detectable quantities), chromatography of normal bovine vitreous filtrate revealed only the presence of the slower-moving fractions.

Discussion

Gradual enzymatic depolymerization of vitreous hyaluronate appears to proceed in two successive stages:

The first yields products of increasing electrophoretic motility corresponding with decreasing chain length, but without releasing reducing substances.

The second period of enzymatic depolymerization, characterized by the liberation of reducing substances, yields products of even smaller particle size as indicated by their fast migration in chromatographic experiments. However, the effect of decreasing particle size on electrophoretic behavior is counteracted by changes in the electrochemical properties of the depolymerization products, probably by the gradual splitting off of glucuronic acid, which was found in free form in fully depolymerized digests.

This splitting off of glucuronic acid by the action of hyaluronidase is shown to be incomplete, the main end-product by hyaluronidase digestion was found to be a disaccharide unit composed of glucuronic acid and acetyl-glucosamine. The susceptibility of this digest to the action of β glucuronidase speaks in favor of the β configuration of the glycosidic linkages.

Summary

Undepolymerized vitreous hyaluronate is characterized by greater electrophoretic motility than that prepared from umbilical cords. Gradual enzymatic (hyaluronidase) breakdown of vitreous hyaluronate starts with the yielding of mucopolysaccharide units of increasing electrophoretic motility without the liberation of reducing substances and glucuronic acid which appear in the second stage of depolymerization. During this period, compounds of decreasing chain length characterized by increasing chromatographic but unchanged or insignificantly decreasing electrophoretic motility are produced. The end-products of the action of hyaluronidase are, in addition to glucuronic acid and acetyl glucosamine, a disaccharide unit, composed of both, susceptible to the action of β glucuronidase.

Department of Ophthalmology.

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MODIFIED IRIDENCLEISIS*

GYULA LUGOSSY, M.D.
Budapest, Hungary

In the operative treatment of glaucoma iridencleisis is gradually increasing in importance. It is expected that technical development and improvements in technique will place this operation in first place among the operations for glaucoma. This view is verified by the increasing number of reports of its successful application.

The modification herein described differs from known methods of iridencleisis in respect to the size of the conjunctival flap, the size of the scleral wound, and the mode of incarcerations of the iris lip. These modifications make the operation more effective and promising in all kinds of glaucoma.

EARLIER METHODS OF IRIDENCLEISIS

The first operation incarcerating the iris was devised a century ago. Since then, it has been repeatedly modified. After the experiments of Bader, Herbert, Treacher-Collins, Critchet, and others, Holth reported in 1905 (Heidelberg) on his modification, named for him, which was quickly adopted as an operation for chronic glaucoma. Later, Pillat devised a modification which made the operation still more efficient. Pillat prepared a conjunctival flap, larger than usual, made a broad incision in the sclera two mm. above the limbus, withdrew the iris with forceps, transected it meridionally with Wecker's scissors, then pulled it—unlike Holth who left it in the midline from which it often fell back—to the end of the wound and laid it below the conjunctival flap. The other part of the severed iris frequently fell back into the chamber, causing an irregular coloboma. Sometimes this part of the iris also adhered to the scleral wound and a pear-shaped coloboma resulted.

Holst reported 455 iridencleises, the results of which were rather good; postoperative pilocarpine instillations were needed by only 12.5 percent of his patients. Progressive functional failure of the eye was halted in 79.8 percent.

The operation to be described leads to results as good as Holth's and Pillat's iridencleisis.

A small iris flap, like one obtained with basal excision of the iris, is drawn into the scleral wound with the pigmented epithelium facing the conjunctival flap.

Other fistulizing operations for glaucoma are numerous and varied. Their history has been discussed in detail by Nordmann and by Allen.

In order to avoid instrument penetration of the anterior chamber, Weekers, et al., instead of a lancet-wound, make an incision, using Gayet's (1882), method, near the limbus. Since 1930, this variety of iridencleisis has been described in several papers by Weekers and Weekers, Hubin, Fanchamps, Bonhomme, Roussel, Mathieu, Heintz and Thibert. In their modifications, the iris prolapsing into the wound is grasped by two Hess' forceps and torn (including the sphincter) into two parts which are tucked in the two ends of the scleral wound, then the conjunctival wound is carefully sutured. Normal tension was obtained and no pilocarpine was needed after operation in 85 percent of acute glaucomas, in 93 percent of subacute glaucomas, 96 percent of chronic glaucomas, and 70 percent of secondary glaucomas.

Djordje and Lukic sever the iris, to preserve its tissues, with Wecker's scissors and tucked it in on one side only. This operation, too, is followed by good results.

Gasteiger and Wagener using Weeker's method obtained excellent results in 94.8 percent of their glaucoma cases. Normal tension ensued in 82.6 percent without, in 6.1 percent with, the help of miotic drugs. In 6.1 percent

* From the Department of Ophthalmology of the State Institute of Rheumatology and Balneology.

the uninfluenced tension was about 15 mm. Hg. Practically, iridencleisis proved a safe operation in all kinds of glaucoma.

Klecker found Weeker's operation so effectively in 89 percent of his patients that he declared that iridencleisis is the operation of choice in cases of glaucoma, in spite of the rarely occurring failures. He emphasizes that later infection and opacities in the lens are rare.

The iridencleisis done by Gayet's ab externo incision and the incarceration of a basal piece of the iris is similarly effective, as seen from the papers of Purtscher, and Sourdille, reporting 78 percent and 93.6 percent good results, respectively.

In a comparative study, Günther and van Beuningen carried out four modifications of iridencleisis with 163 patients suffering from glaucoma: 55 patients were operated by Holth's and Pillat's original method (thorough transection), 15 by tucking a small peripheral iris lip into the scleral wound, 80 by laying, through the ab externo approach, an entire iris flap below the conjunctiva, and 13 by the same method except that only a small peripheral iris lip was used up. None of these methods proved superior to the others. However, gonioscopic findings, from the aspect of a persisting filtration gap, spoke in favor of the ab externo approach, with pinching of a totally transected iris flap into the scleral wound as compared with the original method.

In the opinion of van Beuningen, based on serial gonioscopy, the effect of lowering the intraocular pressure of iridencleisis depends on the size of the incarcerated iris flap as well as of the filtration gap. From this point of view, only the compact incarceration of an intact iris flap (free of adhesions and scars) should be expected to result in normal intraocular pressure. The best point to place a filtration gap, and at the same time the proper place for the incarceration of the iris, lies between Schlemm's canal and the most prominent part of Schwalbe's scleral spur. Filtration scars and the condition of the angle of the chamber are, for the success of iridencleisis, of secondary importance.

Vilmar, too, modified the operation in order to investigate the tension-reducing effect of iridencleisis; he repeatedly examined his patients with the gonioscope before and after the operation. He prepared the wound partly with a lancet, partly ab externo. The iris was pulled out or, in cases of the ab externo method, allowed to prolapse, then it was radially incised down to its radius on both sides of the iris forceps. The flap made in this manner was pinched into the wound. In the majority of cases he incised the pulled-out or prolapsed iris only on one side of the forceps down to its radius, horizontally, toward the temple or the nose, thereby incarcerating a broad second portion. This method has proved more effective. In this way, spontaneous prolapse of the iris takes place and one need not penetrate the chamber with an instrument. Thus, iridencleisis is achieved without an intraocular intervention.

In Vilmar's opinion, the following factors play a prominent part in the tension-regulating effect of iridencleisis:

1. The situation of the filtration gap, the ideal place for which is the area between Schlemm's canal and the scleral spur.

2. The width of the filtration gap, the patency of which is mainly obtained by the duplicate iris flap being pinched in.

Like van Beuningen, Vilmar points out that the size of the filtrating scar and the postoperative width of the angle of the chamber exerts no influence on the tension-regulating effect of iridencleisis.

Weekers and Weekers observed earlier that completely normal tension was also present if the scar was so flat as to exclude, apparently, any filtration. This observation is in contrast with the simple mechanical theory of fistulization and permits the assumption that iridencleisis brings about normal tension by complex neurovascular changes occurring on the anterior uveal surface. The final result is that the activity of the main natural

draining pathways in the anterior uvea increases. Thus, no fistula is needed. If, however, a fistula arises, its effect is an additional factor which contributes to drainage and the tension-lowering mechanism.

Van Beuningen found in four cases that, despite the presence of a filtration scar, iris incarceration, and filtration bleb, the tension remained above normal. He assumes that the operation produces, in such cases, an overpressure outlet. If, however, this outlet is tight, it needs a very high intraocular pressure to function. On the other hand, it is possible that the filtration bleb seems open on gonioscopy, through its deeper part, inaccessible to gonioscopy, has been obstructed as the result of a too oblique incision into the chamber. In this regard, van Beuningen believes that the neurovascular theory of iridencleisis cannot be refuted, yet he is not willing to adopt it, except for those cases in which the deeper parts of the filtration gap are undoubtedly obstructed. This, however, can rarely be revealed by gonioscopy. Therefore, he believes that the open filtration blebs in his patients became engorged deep within and that this accounted for the failure of the operation to decrease tension.

In Barcelona (1958) a report is given by J. Boberg-Ans on 26 operations in 17 glaucoma patients, excluding two reoperations. The operative technique is that of Stallard, with an anterior hinged sclerotomy, cyclodialysis, iridotomy, and iridencleisis. In all except two cases the tension has been normalized without medication; in these two cases, pilocarpine drops are still required.

Present modification and results

By this modification, the original Holth-Pillat operation has been rendered simple and more effective. And, too, the operation can be applied to all cases of glaucoma.

1. Pretreatment

Intraocular pressure is regulated by local miotics and systemic drugs (Diamox or Fonurit, sedatives, and so forth) so that its level is from 30 to 35 mm. Hg at the time of operation. Anesthesia is attained by repeated administration of 0.5-percent Pantocaine into the conjunctival sac, then by the retrobulbar injection of 1.5 to 2.0 ml. of four-percent Novocaine three minutes before the operation. Between the Pantocaine drops instillation of pilocarpine also is advisable, to assure miosis. One or two minutes before operation, one drop of adrenalin (1:1,000) is given. The conjunctival sac is rinsed with a three-percent boric-acid solution, then the lids are washed with benzine and iodine.

2. Dissection of the conjunctival flap

The globe is exposed in the usual way. At the 6-o'clock position 0.2 ml. of a four-percent Novocaine solution is injected below the bulbar conjunctiva. The globe is immobilized with fixation forceps which, facing downward, are held by the assistant. Above the upper border of the cornea the bulbar conjunctiva is inflated by air or (in sensitive patients) with some four-percent Novocaine solution. By means of hooked forceps and curved-bent scissors a semicircular incision is made in the conjunctiva and Tenon's capsule, 10 to 12 mm. above and parallel to the limbus, from the 10-o'clock to the 2-o'clock positions. The conjunctiva is dissected from the sclera. Occasional bleeding from the anterior ciliary vessels is carefully controlled with a thermocautery. The limbus need not be so thoroughly denuded as with Elliot's trephination.

3. Preparation of lancet wound

By means of the fixating forceps the globe is turned downward. The assistant grasps the dissected conjunctival flap with a double hook and raises it slightly to make visible the site of puncture (fig. 1). Then the sclera is pierced obliquely with a broad, curved lancet 1.5 to 2.0 mm. above the limbus. At the same time, the assistant lays the flap on to the lancet, thereby exposing the whole chamber. Then the lancet is directed through the sclera toward the angle of the chamber, the sharp end of the lancet being passed closely in front of the iris until it reaches the junction of the

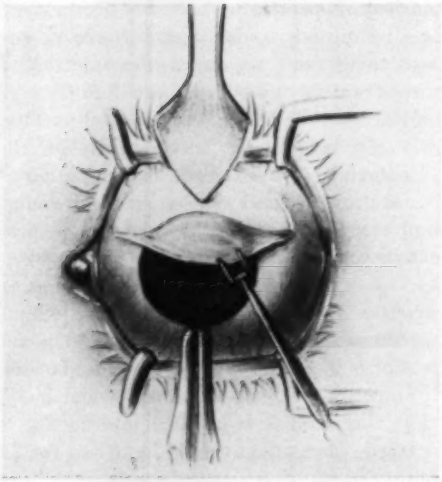

Fig. 1 (Lugossy). The conjunctival flap is retracted and the lancet penetrates the sclera.

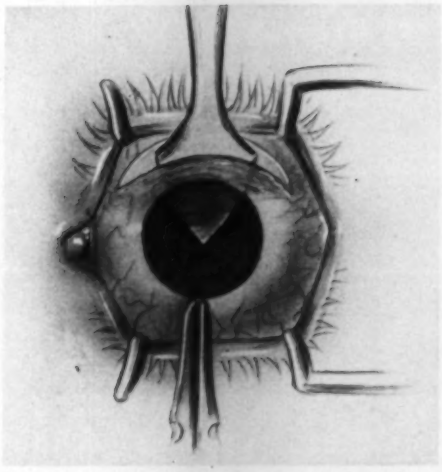

Fig. 2 (Lugossy). The conjunctival flap is replaced and the incision is made with a Landolt lancet.

lower and middle third of the cornea (fig. 2). In this way, the scleral wound has been made larger than in the so-called broad iridectomy. The lower end of the blade of the lancet is held slightly backward, thereby pressing the iris gently backward, until drops of aqueous humor escape. During this process, the sharp end of the lancet is turned a bit sideward. In this way, the escaping aqueous will not sweep the iris away, and the bulging lens cannot come in contact with the point of the lancet. To remove the lancet, its shaft is pressed backward, while its point comes near the posterior surface of the cornea, then it can be slowly withdrawn. If, however, an iris prolapse occurs, it should be replaced into the chamber with a retractor before the operation is continued.

4. Transection and incarceration of the iris

The assistant pulls the conjunctival flap downward with the double-hook to make the wound slightly patent. Now, iris forceps are introduced into the chamber, down to the pupillary margin of the iris, the blades of the forceps are opened for one to two mm. and closed again to grasp a narrow fold of the iris. This fold is elevated through the wound, stretched, drawn to the right toward the end of the wound and cut through toward the iris with Wecker's scissors, the blades of which, while held in the right hand, are gently pressed to the wound (fig. 3). The iris, still held by the forceps, is drawn to the other end of the wound and laid, with its pigmented epithelial surface facing forward, upon the denuded sclera (fig. 4). In this way, two regular coloboma pedicles have been obtained, as after a broad iridectomy, with the difference that one of the coloboma pedicles is free down to its root, whereas the other has been spread into the scleral wound and on the sclera. This procedure keeps it from falling back into the chamber, as in several cases after the Holth-Pillat operation, either early or late postoperatively. The iris section at the right (that having been cut through down to its root) falls back, as a rule, into the chamber. Therefore, the gentle replacement of the coloboma pedicle is rarely necessary.

5. Replacement of the conjunctival flap

The flap is held by a double hook. It should be carefully replaced in a way that the iris section pinched in and spread on the scleral

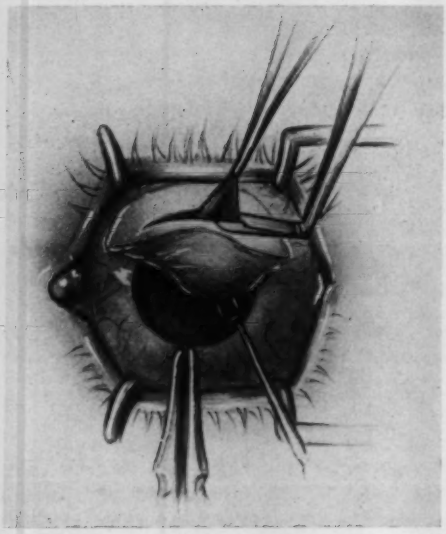

Fig. 3 (Lugossy). The piece of iris is pulled to the edge of the incision and is stretched and transected with Wecker scissors.

wound will be entirely covered by the flap. The flap is replaced to its original position, its wound edges are united with interrupted or interrupted-continuous sutures. Since the pinched iris pedicle has been laid over a large area of the sclera, the wound should be sutured with great accuracy, otherwise undisturbed healing cannot be expected. Before removing the lid retractor, the wound and the coloboma pedicles are once more inspected. If necessary, the iris retractor can be introduced through the closed conjunctival wound into the chamber and the coloboma pedicle can be replaced. The displaced iris lip is seen as a dark translucent spot through the conjunctiva in the prolongation of the scleral wound and a bit laterally (fig. 5). The retractor is then removed, the lower fold of the conjunctiva is cleansed of occasional blood clots, scopolamine is instilled, and the eye is dressed. The patient should lie in bed for 24 hours.

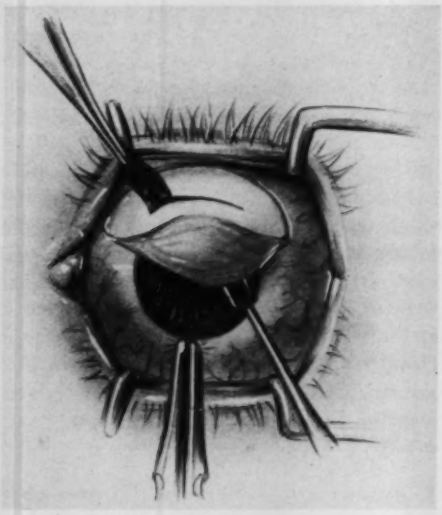

Fig. 4 (Lugossy). The iris is turned back to the other end of the incision and is tucked in and spread out on the sclera.

6. After care

Dressings are changed on the next day. At the same time, scopolamine is instilled in the operated eye, and the patient is allowed to get out of bed. Every morning the eye is bathed with boric acid, scopolamine drops are used and dressings are changed. Conjunctival sutures are removed by the end of the first week, after which dressings are omitted (fig. 6). Scopolamine drops are continued until the chamber is restored and the hyperemia of

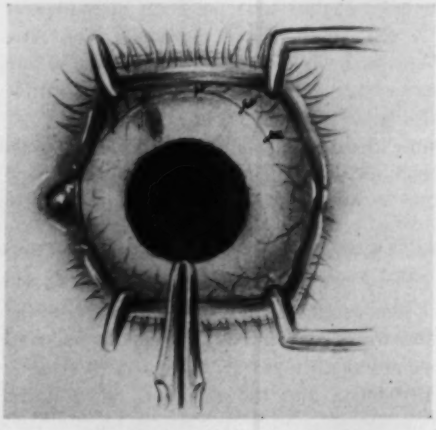

Fig. 5 (Lugossy). The conjunctival flap is replaced and the wound edges are sutured.

the globe begins to decrease and fade.

This management results in the pupillary area of the iris remaining free to react to light. If blood accumulates in the lower part of the chamber, because of bleeding during or after the operation, it should be removed by puncture done simultaneously with the removal of the sutures. If there is blood accumulation in the chamber during the days following corneal puncture, systematic scopolamine is important because hyperemia of the iris may develop into postoperative iritis, and this may give rise to small posterior adhesions at the pupillary edge.

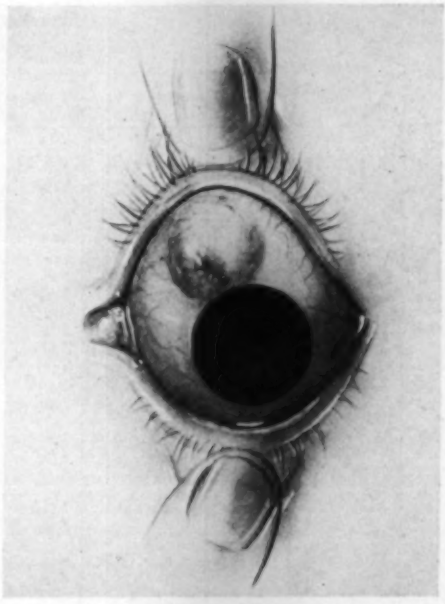

Fig. 6 (Lugossy). A well-functioning filtration bleb after the wound has healed.

7. Results

The modified iridencleisis was performed in this department since early 1955 on 40 eyes of 30 patients. The data of these patients are listed in Table 1. Twelve men and 18 women were operated. Both eyes were operated in 10 patients. There were four cases of glaucoma simplex, seven cases of acute congestive glaucoma, and 19 cases of chronic congestive glaucoma. The age of the patients was between 36 and 87 years.

The intraocular pressure dropped in all patients, irrespective of age and kind of glaucoma. The higher the preoperative tension, the greater the drop. As seen from Figure 7, in two eyes only was the tension over 26 mm. Hg, despite pilocarine. To date, 26 mm. Hg

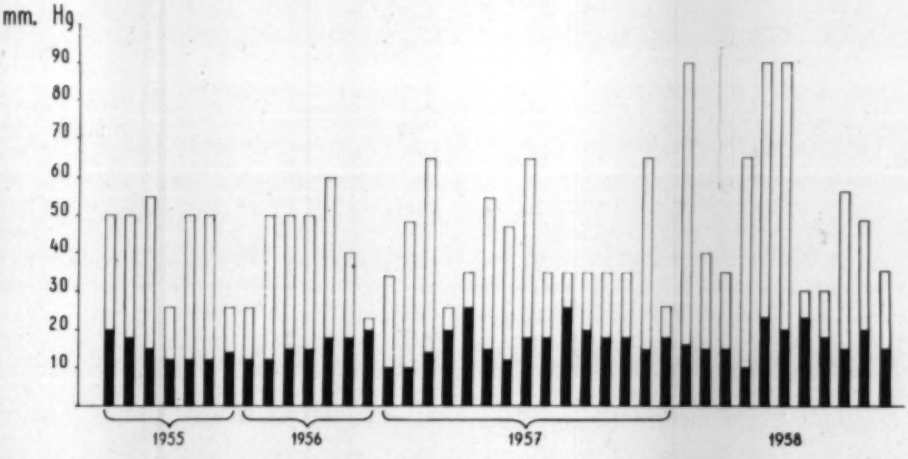

Fig. 7 (Lugossy). Tension values before (light portions) and after (dark portions) the modified iridencleisis.

TABLE 1

SURVEY OF OPERATIONS PERFORMED

No.	Name and Age (yr.)	Diagnosis	Vision	Tension (mm.Hg)	Operation	Time of Control	Vision	Tension (mm.Hg)
			1955					
1	T. E. 74	Gl. congest. chr O.U.	5/6 5/6?	35 50	O.S.	5/ 5/1958	5/6 1 m.f.c.	26 20
2	Z. E. 59	Gl. congest. chr. O.U.	0.5 m.f.c. 5/5	20 50	O.S.	5/ 5/1958	0.5 m.f.c. 5/6	18 18
3	Cs. B. 60	Gl. congest chr. O.U.	5/5 5/5	55 26	O.D.	1/15/1957	5/5 5/5	15 18
4	K. V. 36	Gl. congest. chr. O.U.	5/5 5/5	26 50	O.D. O.S.	1/15/1957	5/5 5/5	12 12
5	Z. I. 60	Gl. cong. ac. O.D., abs. O.S.	1 m.f.c. No l.p.	50 70	O.D.	1/15/1957	5/10 No. l.p.	12 65
6	V. F. 70	Gl. c. chr. O.S., abs. O.D.	No. l.p. 5/8	50 26	O.S.	5/ 2/1958	No. l.p. 5/10	55 14
			1956					
7	M.A. 49	Gl. congest. chr. O.U.	5/15 5/6	26 50	O.D. O.S.	5/ 7/1958	5/10 5/6	12 12
8	D. I. 70	Gl. congest. chr. O.U.	5/8 5/8	50 50	O.D. O.S.	5/ 7/1958	5/10 5/12	15 15
9	Kr. J. 58	Gl. congest. chr. O.U.	H.m. 5/6	60 60	O.S.	5/10/1958	H.m. 5/5	18 18
10	U. K. 60	Gl. congest. chr. O.U.	5/5 5/20	20 40	O.S.	5/16/1958	5/5 5/10	18 18
11	G. E. 53	Gl. simplex O.U.	5/12 5/8	23 20	O.D.	5/11/1958	5/12 5/6	20 20
			1957					
12	M. I. 63	Gl. simplex O.U.	5/5 1 m.f.c.	34 48	O.D. O.S.	4/22/1958	5/8 2 m.f.c.	10 10
13	T. E. 87	Gl. congest. chr. O.U.	5/8 5/10	23 65	O.S.	4/22/1958	5/6 5/15	23 14
14	H. J. 55	Gl. simplex O.U.	5/5 5/5	26 35	O.D. O.S.	4/29/1958	5/5 5/5	20 26
15	D. F. 64	Gl. cong. ac. O.D.	0/5 m.f.c. 5/6	55 18	O.D.	4/29/1958	5/12 5/6	15 20
16	S. J. 65	Gl. congest. chr. O.U.	5/8 No l.p.	47 56	O.D.	3/24/1958	5/10 No l.p.	12 45
17	K. M. 69	Gl. cong. ac. O.S.	5/5 5/12	26 65	O.S.	3/24/1958	5/5 5/6	20 18
18	B. L. 65	Gl. congest. chr. O.U.	5/5 5/50	26 35	O.S.	4/30/1958	5/5 5/10	23 18
19	Cs. G. 69	Gl. congest. chr. O.U.	3 m.f.c. 5/8	35 35	O.D. O.S.	2/26/1958	3 m.f.c. 5/20	26 20
20	H. Gy. 71	Gl. simplex O.U.	5/15 5/6	35 35	O.D. O.S.	5/12/1958	5/10 5/10	18 18
21	T. J. 57	Gl. cong. ac. O.D.	1 m.f.c. 5/8	65 26	O.D. O.S.	5/ 2/1958	5/5 5/5	15 18

TABLE 1—(*continued*)

No.	Name and Age (yr.)	Diagnosis	Vision	Tension (mm.Hg)	Operation	Time of Control	Vision	Tension (mm.Hg.
			1958					
22	G. S. 57	Gl. cong. ac. O.S.	5/6 1/5 f.c.	12 90	O.S.	5/ 3/1958	5/6 5/15	16 16
23	L. J. 64	Gl. congest. chr. O.U.	5/10 5/8	40 35	O.D. O.S.	3/12/1958	5/10 5/8	15 15
24	Ny. M. 61	Gl. cong. ac. O.D.	H.m. 5/8	65 20	O.D.	4/ 2/1958	5/25 5/6	10 23
25	F. P. 70	Gl. congest. chr. O.S.	0.5 f.c.	90	O.S.	5/ 7/1958	— 5/15	— 23
26	Gy. A. 59	Gl. cong. ac. O.S.	5/8 1 f.c.	23 90	O.S.	5/ 7/1958	5/5 5/5	26 20
27	Sz. M. 63	Gl. congest. chr. O.D.	5/5 —	30	O.D.	3/28/1958	5/5 —	23 —
28	K. T. 63	Gl. congest. chr. O.U.	5/5 5/5	26 30	O.S.	3/12/1958	5/5 5/6	20 18
29	P. F. 78	Gl. congest. chr. O.U.	No. l.p. 5/20	56 48	O.D. O.S.	4/ 9/1958	No l.p. 5/40	15 20
30	T. B. 69	Gl. congest. chr. O.U.	5/20 5/10	35 23	O.D.	5/23/1958	5/12 5/10	15 18

has been regarded as the upper limit of normal tension. However, Weekers, Watillon, and de Rudder point out that, on the base of American standards and the Schiøtz tables edited by the American Academy of Ophthalmology in 1954, intraocular pressure is physiologic between the limits 10 and 22 mm. Hg, and 15 to 16.5 mm. should be regarded as entirely normal.

For this reason pilocarpine was prescribed for all dismissed patients, if the postoperative tension was 20 mm. Hg or more. In Figure 7, tension values are represented by the black areas on the day of the last examination.

The application of pilocarpine reduced all tension levels of 20 mm. Hg or more to about 18 mm. Hg except for the two cases already mentioned. The greater postoperative effect of pilocarpine is, in my opinion, a sign of a successful iridencleisis.

Of course, the 30 eyes in which tension was 12 to 18 mm. Hg after operation without the use of pilocarpine, are better evidence for the effectiveness of the operation. In these cases a large filtration scar arose around the incarcerated and subconjunctivally displaced iris lip. In contrast to this, a filtration scar developed in the eyes with 20 to 26 mm. Hg tension very slowly if at all. Gonioscopy revealed a broad filtration bleb in the former cases, a narrow one or none in the latter cases.

Significant changes in visual fields cannot be observed until a long time after operation. Therefore, the visual field data presented in Table 1 were collected at the follow-up examinations carried out three, two, and one year after operation. These examinations have shown that there is a close parallel between intraocular pressure and visual fields. Those visual fields that were normal at the time of operation did not change within three years even in cases with 26 mm. Hg postoperative tension. Those visual fields which were more or less contracted at the time of operation, increased only in those patients whose intraocular pressure did not exceed 20 mm. Hg

after the operation. In patients over 70 years of age and suffering from sclerosis, glaucoma-induced contraction of the visual field is more likely than at a young age. As seen, for example, Table 1 Case 1, if there was contraction at the center of the field before operation, the contraction became complete soon after the operation and central sight was completely lost. In 90 percent of the eyes operated by the modified iridencleisis, the visual field did not change essentially after operation.

Vision became worse only in one of the operated patients because of the loss of central vision. In the majority of my patients vision did not change after operation, except in patients operated for acute congestive glaucoma, in several of whom central vision, seemingly lost, returned. In a few patients refraction changed toward myopia. In four patients opacities of the lens increased after operation and gave rise to diminished vision.

Neither during nor after operation did complications occur. Postoperative bleeding filling the inferior third of the chamber occurred in two patients. Blood was removed by puncture. In some cases wrinkles in Descemet's membrane, due to the drop in tension, were observed. These wrinkles interfere with visual acuity. Their resolution takes a long time and preoperative vision cannot be restored earlier. The increase of opacities in the lens was never so extensive as to necessitate a cataract operation.

Discussion

From the results of the modified iridencleisis herein described, it may be concluded that the effectiveness of the operation depends on several factors: (1) Site and size of the scleral incision; (2) method and extension of incarcerating the iris; (3) extent and duration of filtration; (4) absence of complications.

1. Since the success of the operation depends chiefly on the site and size of the scleral incision, the site should be selected before operation by careful study with slit-lamp and gonioscope. After the proper place has been found (1.5 to 2.0 mm. above the limbus), Landolt's lancet should be introduced in such a manner that the instrument reaches the chamber directly at the base of the iris. Gayet's incision is indicated only if the chamber is excessively narrow. The incision made with a lancet is larger and more even than that obtained by Gayet's incision. For an effective iridencleisis a scleral incision of eight to 10 mm. in length is needed, depending on the diameter of the cornea.

If the scleral wound is adequate, broad iridencleisis can be accomplished without stretching the iris lip, diminishing the danger of its atrophy (Purtscher).

Gonioscopic examinations after successful iridencleisis operations (stabilizing intraocular pressure at 12 to 18 mm. Hg) have shown that the filtration bleb forms close to Schlemm's canal. In these cases a large filtration bleb and a large filtration scar had developed, and intraocular pressure, even after several years, did not exceed 18 mm. Hg, though no miotic drugs were given.

On the other hand, in cases in which tension exceeded 20 mm. Hg the cause of insufficient filtration could invariably be found with the gonioscope. For instance, in Case 29 (table 1) the scleral incision in the left eye was too close to the limbus and the iris flap underwent cicatrization; therefore the aqueous humor is insufficiently drained, and normal tension cannot be maintained without pilocarpine. In Cases 1, 9, 14, and 19, the narrowness of the filtration gap was due to the fact that the scleral wound was not made large enough. In Cases 25 and 29 the incarcerated iris slip was not sufficiently broad.

2. The effect of the operation is determined by the broad incarceration of the iris. Many failures of iridencleisis and its earlier modifications can be explained by the insufficiency of incarceration. The one iris lip may have fallen back into the chamber, or it may have adhered to the wound edges without partaking in fistula formation. Therefore, I cut through the stretched out iris lip, drawn

to the end of the scleral wound, down to its root, as in broad iridectomy. Then the lip is, by means of the iris forceps, turned over to the other end of the wound, and spread wide out below the conjunctiva, with the pigmented epithelial surface in front. In this way, wide pinching is achieved without stretching the iris. Tucking is broad because I cut through only one half of the extracted iris lip with Wecker's scissors, while the other half is turned with its pigmented epithelium facing forward to the other end of the wound. After severing, the coloboma pedicle falls back into the chamber, or it is carefully replaced with a spatula. The efficiency of this modified iridencleisis is still further augmented by the effect of iridectomy plus fistula formation.

This technique of incarceration with the pigmented epithelial coat facing the bulbar conjunctiva is an important factor for good filtration because it prevents cicatrization. This role of the pigmented epithelial surface of the iris was emphasized early by Holth. Recently, it has been pointed out by Reese and Maggiore. It is by the careful employment of the pigmented epithelium that the modified iridencleisis results in good filtration from the anterior chamber directly into the subconjunctival space.

To prevent cicatrization in the subconjunctival space in the region of the tucked iris flap, Laval applied an absorbable gelatine film (4:10 mm. gelfilm) to the scleral wound, then he carefully sutured the conjunctiva and Tenon's capsule over the film. The gelfilm was visible below the conjunctiva for two to four months. After its absorption, a large filtration scar free of any reaction developed in 21 of 24 cases. In three cases in which the scar was small and flat, the filtration was, however, excellent, as demonstrated by the low tension. In my modification, the use of a gelfilm or any other substance to prevent scar formation is superfluous because the formation of a well-functioning filtration scar is best obtained by the way of managing the iris lip, as has been described.

3. The efficiency of modified iridencleisis may also be ascribed to good and lasting filtration. I do not claim that a large filtration scar was a consistent phenomenon in my successful operations; there was also lasting low tension without it. It is, however, quite certain that a broad and bulging filtration scar was invariably attended by lasting low tension (Cases 4, 5, 7, 12, and 16 etc.).

Sourdille points out that in his cases operated with unsatisfactory results the filtration scar was, if at all present, very small. Meyer denied the significance of fistula formation. Günther and van Beuningen are, on the basis of gonioscopic examinations, of the opinion that the filtration bleb is a more important factor than the conjunctival scar. My gonioscopic examinations seem to demonstrate that broad incarceration secures a good filtration bleb, and the latter results in the formation of a large filtration scar.

Weekers and Weekers, too, mention that, after iridencleisis, extremely low tension was not always present in those eyes in which the postoperative scar was extremely large and edematous. Low tension (18.3 mm. Hg) was associated with a flat scar as well as with a larger vesicular scar. Very low tension (12.9 mm. Hg) occurred in the presence of a cystic filtration scar. Irrespective of the aforementioned cases, Weekers and Weekers contend that iridencleisis diminishes intraocular pressure through complex neurovascular changes taking place at the level of the anterior uvea. My modification promotes these neurovascular effects by the partial iridectomy. Dieter reported, as early as in 1942, that afferent pathways start from the uvea.

The study of the aqueous veins has shown that the drop of tension following iridencleisis cannot be interpreted as due to increased drainage through these veins. The veins are visible after operation less than before. Weekers and Weekers disclosed them in only 24 of 45 cases. François confirmed these observations.

Caselli as well as Cristini and Pentini discarded the role of filtration after iridencleisis,

on the basis of rabbit experiments. They assume that influences exerted on the anterior uveal zone by the sympathetic-parasympathetic pathways, resulting in decrease of pressure in the venous capillaries of the uvea, play a prominent part.

4. The good results obtained by the modified iridencleisis are, beyond any doubt, partly due to the absence of complications. Pillat mentioned the following complications which may impair the results:

a. *During operation:* perforation of the conjunctival flap, too small flap, improper (too short or too long) distance between limbus and scleral wound, injury to the lens, tear of iris, its detachment from its basis, dislocation of lens, expulsive hemorrhage.

b. *During healing:* Lasting narrowness of the chamber, detachment of the uvea, periodic pains in the globe.

c. *Late complications:* Iritis, sympathetic ophthalmia, infection of the filtration bleb, increase of tension, extension of the scleral scar.

Kalt, Decaudin and Loisillier observed after iridencleisis a more or less prolonged iritis in 77 percent of their patients. Kalt, Decaudin and Krajevitch attribute this iritis to the operation trauma. To prevent it, Weekers was the first to suggest Gayet's incision for the scleral wound. A patient of Klecker developed, three days after iridencleisis, a vitreous abscess which was followed by panophthalmitis and the loss of the eye. The same occurred in a patient of Lewis seven years after the operation. Holst and Iliff reported on sympathetic ophthalmia, one case each. Hoffman-Egg observed sympathetic ophthalmia (verified by histology) six months after the operation. Mackie and Rubinstein reported on two cases of sympathetic ophthalmia in 110 operations. This severe complication did not occur in any of my cases.

In my 40 cases, hypertrophy of the filtration scar (Reichling) did not ensue either. In a patient of Lewis the filtration scar became so large in two years that it overhung the limbus for 4.5 mm. and its partial removal became necessary because of the erosion of the cornea. In two cases of Klecker the hypertrophy needed no treatment.

It is just the rarity of complications that makes iridencleisis superior to other glaucoma operations. Because of the rare incidence of infections and opacities in the lens, iridencleisis is to be particularly preferred to Elliot's trephination.

Fanta undertook a comparative study on 216 trephinations and 135 Holth's iridencleises. He observed the clearness of the lens after trephination in 40 percent, after iridencleisis in 87.4 percent. The opacities were due chiefly to postoperative iritis. Dellaporta observed 11 late infections after Elliot's trephination, while iridencleisis was performed in 224 cases without a single late infection. He reviewed the literature of iridencleisis and found only six late infections among 2,048 reported cases.

Brauswetter-Köppner states that the percentage of late infection after trephination is 6.65 percent, after iridencleisis practically zero. Wagener observed opacities of the lens in 46 of 120 trephination cases, whereas iridencleisis was rarely followed by such opacities. Klecker mentioned that traumatic cataract occurred only once in the course of 165 iridencleisis operations and this was caused by a small mistake in technique.

Conclusions

The excellent results obtained by the modified iridencleisis are in full harmony with the extensive comparative statistical studies which speak in favor of the advantages of iridencleisis in comparison with other operations for glaucoma (Nonnenmacher, Wagener, Wehner, Böhringer and Koenig, Agarwal, and others). Owing to its simple technique, the modified iridencleisis herein described can be achieved always perfectly, resulting in reduction of intraocular pressure to normal, preservation of vision and visual fields. The modified iridencleisis was performed on 40 eyes of 30 patients. The ten-

sion decreased, though to varying extents, in all cases; therefore, wide application of this operation seems to be justified.

Iridencleisis has proved effective in both closed-angle and open-angle glaucoma (Hill, Klecker, and others). The operation has proved effective in secondary glaucoma (Kalt, Sourdille, Weekers, Gildemyn, Vilmar), and also in congenital glaucoma (Weekers, Kalt, Farnarier and Sobrepère, Klecker, Law). Since the indications for iridencleisis are so numerous, it is conceivable that it should be preferred to all other operations aiming at the reduction of tension in all forms of primary and secondary glaucoma.

The chief advantage of iridencleisis as compared with other operations for glaucoma is that the number of complications is considerably lower after iridencleisis. It may suffice to point to the inflammatory processes following cyclodialysis, or to the late infections and cataract formation observed after Elliot's trephination.

In my cases no complication whatever attended the modified iridencleisis. With my modification the operation has been made more simple and more effective. The size of the scleral wound allows the broad tucking of the iris. The transection of the half of the iris lip down to its root before tucking secures a regular coloboma pedicle free of scars and constitutes an additional factor (iridectomy) by which the outcome of the operation is improved. The broad incarceration of the other half of the iris lip and its spreading out on the sclera, along with the transected part, with the pigmented coat facing the conjunctiva, bring about an excellent filtration from the angle of the chamber toward the subconjunctival space, thereby attaining in the majority of cases a rather low tension (from 10 to 18 mm. Hg) without the use of miotic drugs.

Gonioscopic examinations have shown that the best place for the scleral wound is in the area neighboring Schlemm's canal. If the operation is accomplished here, the complex neurovascular changes occurring in the anterior uvea are activated and their effect is still further increased by the suggested partial transection of the iris.

Summary

A modified iridencleisis resulted (30 patients, 12 males and 18 females) in lasting normalization of ocular tension. The modification combines iridencleisis and iridectomy.

After dissecting a large conjunctival flap, an incision eight to 10 mm. in length is prepared on the sclera 1.5 to 2.0 mm. above the cornea, Gayet's incision being used if the chamber is narrow. As in broad iridectomy, the iris is extracted, stretched, then one half is cut through to the base and laid, with the pigment epithelial surface facing the sclera, on the sclera, while its end is fixed at the other end of the scleral wound where it is carefully sutured with interrupted or interrupted-continuous sutures. In 90 percent of the operated cases the vision has been unchanged for several years, in 70 percent without the administration of miotic drugs. Since this modified iridencleisis has been successful and without complications, it can be performed in all kinds of glaucoma.

Frankel Leó-u. 17-19 (II).

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CONTRACTION OF THE OCULOROTARY MUSCLES AND INTRAOCULAR PRESSURE*

A TONOGRAPHIC AND ELECTROMYOGRAPHIC STUDY OF THE EFFECT OF EDROPHONIUM CHLORIDE (TENSILON) AND SUCCINYLCHOLINE (ANECTINE) ON THE INTRAOCULAR PRESSURE

WALTER KORNBLUETH,† M.D.
Jerusalem, Israel
AND
ARTHUR JAMPOLSKY, M.D., EDWARD TAMLER, M.D., AND ELWIN MARG,‡ PH.D.
San Francisco, California

Numerous studies have shown that contraction of the oculorotary muscles increased the intraocular pressure.[1–5] The effect on the ocular tension was found to be similar if the muscles were stimulated mechanically, electrically or chemically.

The purpose of this paper is to show that an increase in the tonus of the oculorotary muscles is associated with and may be the cause of a rise in intraocular pressure and that the increase in intraocular pressure is proportional to the degree of contraction of the oculorotary muscles.

MATERIAL AND METHODS

Tonographic and electromyographic measurements were performed simultaneously in 10 patients. The patient was put on a table in an electrically shielded cage made of copper window screening. The electromyographic technique used here and the interpretation of electromyograms are described in detail elsewhere.[6,7] In all the cases the electrodes were inserted into the horizontal or vertical recti of one eye, recording agonist and antagonist simultaneously. An electronic tonometer with a 5.5-gm. weight was used. This was attached to a recorder outside the shielded cage; the wire connecting the electrically insulated tonometer handpiece with the amplifier was led into the cage through a small hole in the screen. In two normal patients, and in three patients with limitation of eye movements due to myasthenia gravis, continuous electromyographic recordings were made for the duration of the experiment. The patients with myasthenia gravis discontinued drugs at least 24 hours before the test. The tonometer was placed on one eye, and after a tonography of one to two minutes' duration, 10 mg. of edrophonium chloride was injected intravenously and the tension recorded for a few minutes thereafter without removing the tonometer from the cornea. The same procedure with an additional injection of 10 mg. of edrophonium chloride was repeated five to 10 minutes later on the second eye.

In five normal subjects, succinylcholine in varying amounts (5.0 mg., 10 mg., 15 mg., 20 mg.) was injected intravenously while electromyography combined with tonography were performed as described above. All patients received a small amount of demerol as premedication, and two patients were given regulated Plane I general anesthesia with pentothal sodium.

OBSERVATIONS

Edrophonium chloride did not alter the electrical activity of the oculorotary muscles (in normal patients), nor the usual smoothly declining curve of tonography (fig. 1). Patients with myasthenia gravis showed a moderate increase of activity of the oculoro-

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† Department of Ophthalmology, Hadassah Rothschild University Hospital, Jerusalem, Israel.
‡ School of Optometry, University of California, Berkeley.

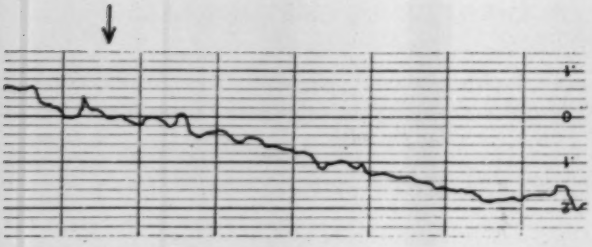

Fig. 1 (Kornblueth, et al.). Tonographic record of normal subject, showing no change in intraocular pressure following intravenous injection of 10 mg. of edrophonium chloride (Tensilon). Time is one-half minute between vertical lines.

tary muscles tested approximately 20 to 30 seconds following the injection of edrophonium chloride, and coinciding with this change of muscle activity there was a rise of 2.0 to 4.5 mm. Hg in the tonogram (figs. 2A and 3A). The intraocular pressure decreased after one-half minute in spite of continuous higher electrical activity of the oculorotary muscles (fig. 3B). The second injection of 10 mg. edrophonium chloride, repeated five to 10 minutes later for measurement of second eye, caused a much smaller increase of both the electrical activity of the muscles and of the intraocular pressure (fig. 2B).

Succinylcholine produced some enophthalmus in all patients appearing 20 to 30 seconds following the injection. None of the subjects became apnoeic and there was no need for artificial respiration. There was a rise in intraocular pressure coinciding with the appearance of the enophthalmus, which was less in the patients under general anesthesia, 2.0 to 4.0 mm. Hg (fig. 4), than in the fully conscious patients, 5.0 to 14 mm. Hg (fig. 5). It seemed that the duration of increase in intraocular pressure, rather than the amount of increase, was related to the dosage of the drug administered. The rise in ocular tension occurred at the moment the electrical activity of the oculorotary muscles became extremely small. There was no sudden burst of electrical activity of the oculorotary muscles immediately before the onset of electrical silence of these muscles (fig. 6).

Discussion

Edrophonium chloride (Tensilon)

This product, an analogue of neostigmine, is a rapidly acting cholinergic drug and is characterized by prompt, brief action in patients with myasthenia gravis.[5-9] The response consists of a temporary increase of muscle strength within one-half to five minutes following an intravenous injection. It causes fasciculations in normal patients without increase in muscle strength.

The increase in electrical activity of oculorotary muscles in patients with myas-

Fig. 2 (Kornblueth, et al.). (A) Tonographic record of a subject with myasthenia gravis, showing increase in intraocular pressure following intravenous injection of 10 mg. of edrophonium chloride (arrow). (B) Tonographic record of other eye of same subject as in Figure 2A, showing smaller rise in tension following a second injection of 10 mg. of edrophonium chloride approximately five minutes after the first injection.

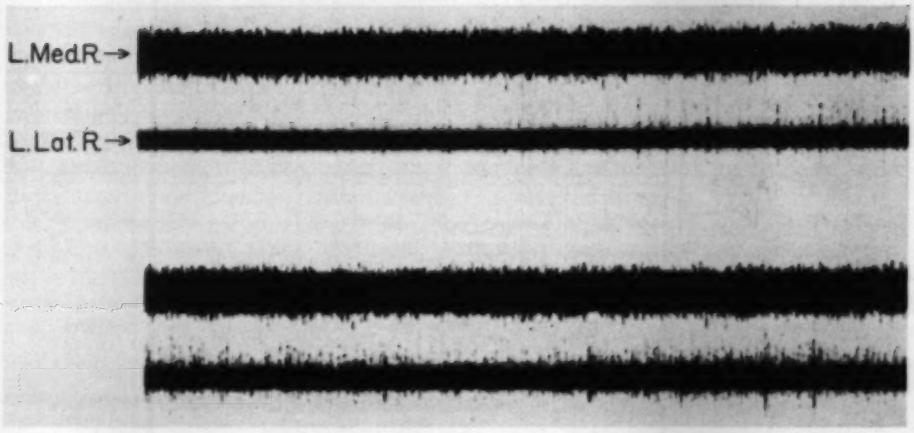

Fig. 3A (Kornblueth, et al.). Same subject as in Figure 2A, showing increasing activity of the left lateral rectus and no significant change in the antagonist left medial rectus which indicates no eye movement following intravenous injection of 10 mg. of edrophonium chloride. [This is a continuous record.] The increased activity coincided with the rise in intraocular pressure seen in Figure 2A.

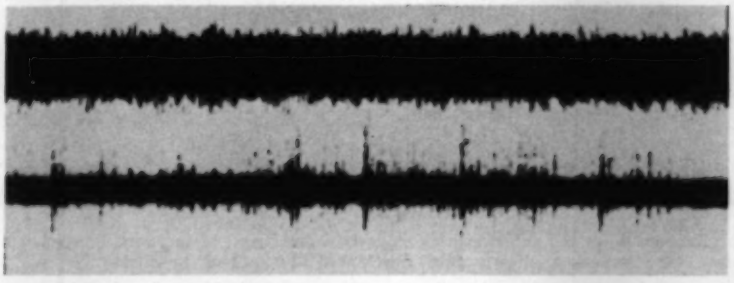

Fig. 3B (Kornblueth, et al.). Two and one-half minutes after intravenous injection of edrophonium chloride in same subject showing maintained increased activity of left lateral rectus, during which time the intraocular pressure was decreasing.

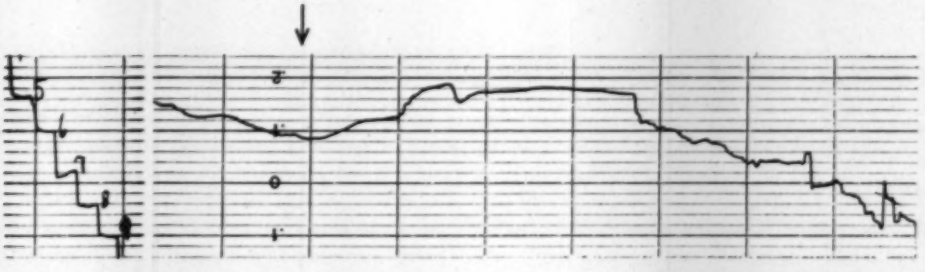

Fig. 4 (Kornblueth, et al.). Tonographic record of a seven-year-old subject under general anesthesia, showing small increase in intraocular pressure following intravenous injection of 5.0 mg. succinylcholine (arrow).

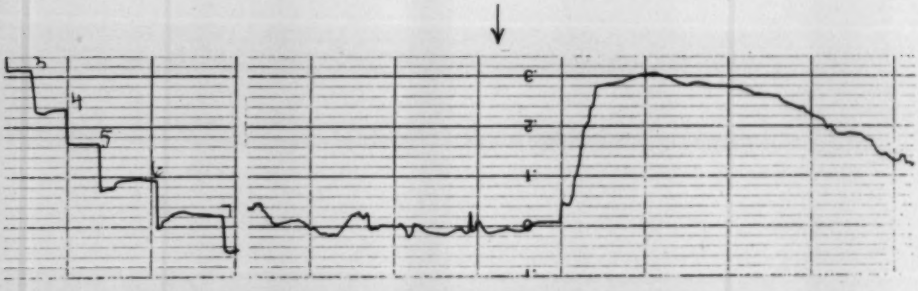

Fig. 5 (Kornblueth, et al.). Tonographic record of a fully conscious patient, showing a marked increase in intraocular pressure following intravenous injection of 5.0 mg. of succinylcholine (arrow).

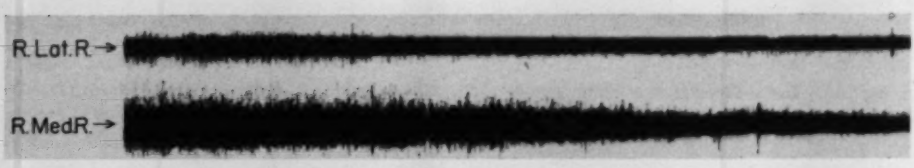

Fig. 6A (Kornblueth, et al.). Decreased activity in horizontal recti 30 seconds after intravenous injection of 10 mg. succinylcholine.

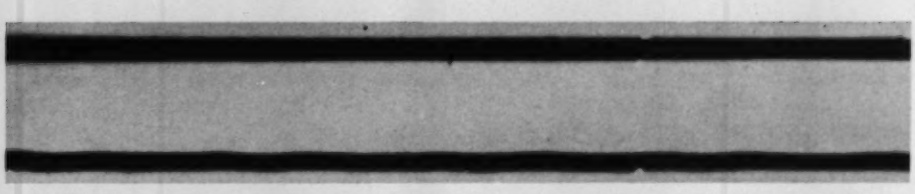

Fig. 6B (Kornblueth, et al.). Electrical silence in horizontal recti of same subject approximately 60 seconds after intravenous injection of 10 mg. of succinylcholine.

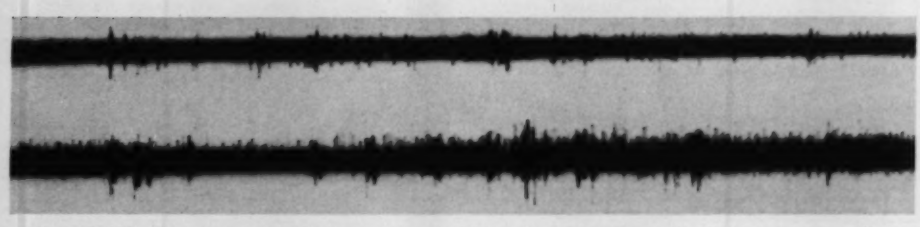

Fig. 6C (Kornblueth, et al.). Shows return of activity in horizontal recti muscles of same subject approximately two minutes after intravenous injection of 10 mg. of succinylcholine.

thenia gravis following an injection of edrophonium chloride was described previously.[10,11] It was stated that increased activity was not necessarily accompanied by much or any improvement of ocular motility.

Our study confirmed the demonstration of a moderate increase in the electrical activity of only those oculorotary muscles which showed a lowered activity before the injection of edrophonium chloride. Increase of electrical activity of the oculorotary muscles was accompanied by a moderate rise of

intraocular pressure which subsided after one-half minute in spite of continued higher electrical activity, of the oculorotary muscles. The rise in intraocular pressure might be explained by the sudden increase of the oculorotary muscle tonus. Consequently, more aqueous humor is expelled from the eye through the normal outflow channels, and the eye apparently adjusted readily to the changed muscle tonus. There was only a slight increase of electrical activity of the oculorotary muscles, and of the ocular tension, following the second injection which was given five to 10 minutes after the first injection and before the effect of the first injection had completely subsided. In normal subjects, there was no rise in intraocular pressure, and following the edrophonium chloride injection, there was no demonstrable change in the recorded electrical activity of the oculorotary muscles.

Succinylcholine

This agent, a competitor of acetylcholine, blocks the myoneural junction by depolarizing the motor endplate of the muscle and is not destroyed as rapidly as acetylcholine. It causes a temporary flaccid paralysis of the skeletal musculature, and because of this action it is widely used in general anesthesia and general surgery.

The oculorotary muscles react differently to succinylcholine than the general skeletal musculature. The oculorotary muscles show either a contraction or a sustained contracture. Excellent studies on man and experimental animals [12-19] showed that a steep rise in intraocular pressure (amounting to as much as 38 mm. Hg) was due to a contraction or contracture of the oculorotary muscles. This finding is evidenced by the appearance of enophthalmus and immobility of the globe following an injection of succinylcholine. Small doses of this drug in experimental animals produced a tetanic contraction while higher doses caused a contracture of the oculorotary muscles.[18] (A contraction of the oculorotary muscles is evidenced by an increased muscle tension and an increased electrical activity. In contracture the development of marked muscle tension is attended by complete absence of electrical activity of the muscle.) The steep instant rise (fig. 5) in intraocular pressure was most probably due to strong mechanical pressure on the globe produced by the marked contracture of the oculorotary muscles tested. In deep anesthesia, which customarily produced electrical silence of all oculorotary muscles, succinylcholine did not induce any electrical activity in this state.

Our study confirmed previous findings that the rise in intraocular pressure was less marked in patients under superficial general anesthesia (who had little electrical tonus as a result of the anesthesia) than in conscious subjects (who had normal electrical tonus). The amount of the drug did not necessarily determine the amount of rise of the intraocular pressure. Previous electromyographic studies by others, of the effect of succinylcholine were performed in man and experimental animals during general anesthesia only.[17, 18, 20]

In the present study electromyography was done on conscious patients following an injection of succinylcholine and the electrical activity of the oculorotary muscles was correlated with the rise in intraocular pressure by simultaneous tonography. Our electromyographic findings are not in complete agreement with those described previously. In all our cases tested the rise in intraocular pressure coincided with the occurrence of electrical silence of the oculorotary muscles. The initial burst of increased electrical activity (before electrical silence) found by others was not seen in any of our cases.

One possible explanation for this discrepancy lies in the different technique employed. Whereas we use simultaneous, multichannel recordings of agonist-antagonist pairs of muscles, other investigators have often used single channel recordings. With simultaneous multichannel recordings one can easily distinguish a co-activity of muscle groups as

compared to a rotation of the eye which is evidenced by an increased electrical activity of the agonist and a reciprocal reduction of activity of the antagonist. An increased electrical activity in the one recorded muscle when one channel only is used, could therefore be a part of co-activity or simply an eye rotation often found shortly after an injection of succinylcholine before the eye is fixed in position by the contracture of the oculorotary muscles.

The different effect of edrophonium chloride and succinylcholine on the duration and amount of rise in intraocular pressure might have the following explanation. Edrophonium chloride caused a moderate increase in the tonus of the oculorotary muscles, and the eye adjusted easily to the new situation in spite of continued increased activity of the oculorotary muscles. Succinylcholine caused the whole globe to be squeezed by the mechanical force of marked muscle contractures, and aqueous humor could only be pushed out through the outflow channels when the muscles started to relax and to release the squeeze. Thus two different drugs with similar action on the oculorotary muscles caused changes in the intraocular pressure according to the degree of contraction of the oculorotary muscles produced by these drugs.

Summary

The effect of edrophonium chloride (Tensilon) and succinylcholine (Anectine) on the state of contraction of the oculorotary muscles and its influence on the intraocular pressure were studied with the aid of electromyography and tonography. It was found that edrophonium chloride, which increased the activity of the oculorotary muscles only in patients with myasthenia gravis, produced a moderate rise in intraocular pressure coinciding with the increased tonus of the oculorotary muscles. In normal subjects no demonstrable change in electrical activity of the oculorotary muscles, and consequently no change in the intraocular pressure, was seen. Succinylcholine which produced a marked contracture of the oculorotary muscles, as evidenced by electrical silence at the height of the effect of the drug, caused an appreciably greater increase in intraocular pressure in conscious normal subjects.

It was shown that the two different drugs, one producing a contraction, and the other a contracture of the oculorotary muscles caused a change in intraocular pressure corresponding to the degree of shortening of the oculorotary muscles produced by each of these drugs.

Hadassah Rothschild University Hospital. Stanford University Hospitals (15).

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EXPERIMENTAL LAMELLAR HETEROGRAFTS*

Comparison of Fresh and Preserved Donor Corneas

Shankar B. Chavan, M.D., and John Harry King, Jr., M.D.
Washington, D.C.

Lamellar corneal transplantation, now being widely applied, is recognized as a valuable therapeutic aid in corneal diseases, particularly in the chronic form of herpetic keratitis.[1] The successful use of corneas preserved by dehydration in glycerine has shown that the problem of supply of corneas for the lamellar type of keratoplasty can be solved if sufficient human corneas can be obtained for prolonged storage.[2-4] The inadequate supply of human donor corneas, however, has indicated a need for reinvestigation of the possibility of utilizing animal corneas, either fresh or preserved for heterogenous grafts.

Many attempts were made during the 19th century to graft animal corneas into human corneas. Most efforts were unsuccessful so far as clarity of the graft was concerned, although many of these transplants were tolerated, remained in place, and healed structurally.[5] In addition to immunologic factors, infections, inadequate instrumentation and surgical techniques, and the lack of anesthesia, may have contributed to many of these failures.

Babel and Bourquin[6] have reported clear interlamellar heterografts in rabbits from ox, sheep, horse, pig, rabbit and human beings. Choyce[7] also reported success with interlamellar corneal heterographs of cat and human corneal tissues in rabbits which united with the host tissue and remained transparent for prolonged periods.

Heuven[8] reported successful nonpenetrating heterografts from fresh cat cornea to rabbit, human to goat, and rabbit to dog. Basu and Ormsby[9] used both interlamellar and lamellar techniques for corneal heterografts in rabbits, utilizing fresh avian and mammalian donor tissues. They concluded

* From the Department of Surgery, Georgetown University Medical Center, and the Department of Ophthalmology, Washington Hospital Center. This investigation was supported in part by the Lions of District 22-C Eye-Bank and Research Foundation, Inc., Washington, D.C., and by Research Grant, B-975(R) and B-2062, from the National Institute of Neurological Diseases and Blindness of the National Institutes of Health, Public Health Service, Bethesda, Maryland.

that antigen-antibody reactions occurred in all donor tissues, but these were less frequent with avian corneas than with mammalian corneas. The use of chicken corneas resulted in fewer reactions than either those seen with duck or turkey corneas. Reactions with the use of monkey corneas occurred less frequently than those with lamb or beef.

Rycroft[10] expressed the opinion that heteroplasty must not be entirely dismissed. He mentioned that there was no evidence to show how heterografts would have behaved if they had been preserved.

Present studies

Animal experimentation was performed to study the behavior of preserved lamellar heterogenous grafts and to compare these with results obtained from fresh donor corneas. Histopathologic observations were made to determine which type of donor material would be least antigenic. If opacification occurred it could usually be explained on the basis of an antigen-antibody reaction.

Procedures

Animal and human corneas were preserved by dehydration in glycerine according to the method previously reported.[3,4] An equal number of fresh and preserved corneas were grafted at various intervals by the lamellar techniques from human, horse, monkey and dog, to cats and cat to dogs (table 1).

Full-grown animals with normal corneas were used as recipients. They were anesthetized with intravenous pentobarbital (Nembutal) and the procedures were performed under sterile conditions. The technique of lamellar grafting was the same as that previously reported,[3] except that the donor corneas were rehydrated for 15 minutes in sterile saline antibiotic solution containing polymyxin B, neomycin, and gramicidin* and a corneal clamp[11] was used to fix the preserved donor corneas while the lamel-

* Neosporin®, Burroughs Wellcome and Company, Inc., Tuckahoe, New York.

TABLE 1

Fresh and preserved lamellar heterografts*

Donor Tissues	Number of Grafts		Storage Time		Graft Size (mm.)	Average Graft Status (gross and microscopic)		Postoperative Graft Age (weeks)
			P					
F and P	F	P	(yr.)	(mo.)	F and P	F	P	F and P
1. Human	9	9	1	11	5	4	5 Clear	9
						3	3 Partly opaque	12
						2	1 Opaque	14
2. Horse	9	9		4	5	3	4 Clear	9
						3	3 Partly opaque	12
						3	2 Opaque	14
3. Monkey	9	9	1	1	5	3	4 Clear	9
						4	2 Partly opaque	12
						3	3 Opaque	14
4. Cat	9	9	2	6	5	2	3 Clear	9
						4	3 Partly opaque	12
						3	3 Opaque	14
5. Dog	9	9	2	6	5	1	2 Clear	9
						4	3 Partly opaque	12
						4	4 Opaque	14

* Based upon gross and microscopic findings (table 2).
F = fresh; P = preserved (corneas preserved by dehydration in glycerine).

lar dissection was being completed. For the first three postoperative days all animals received 150,000 units of penicillin intramuscularly daily. An antibiotic ophthalmic solution* was instilled in the operated eye each day for one week following this period. The silk corneal sutures were removed on the 10th postoperative day.

The eye operated upon was observed grossly and with slitlamp examination each day, and a notation was made of the clarity of the graft as well as the character and intensity of the postoperative reaction. On the 10th day the animals were classified into three groups depending upon the type of postoperative inflammatory reaction and the clarity of the grafts. Each group was treated daily by local instillation of a prednisolone-antihistamine preparation,† cyclopentolate hydrochloride (0.5 percent),‡ prednisolone-neomycin ointment.‖

Five types of profiles and features of immunologic donor-recipient reactions and clarity of the grafts were graded from 0 to 4 plus. These were based upon the degree of ocular inflammation: (1) conjunctival congestion, (2) corneal edema, (3) neovascularization, (4) opacification, and (5) iritis.

The postoperative reactions and the clarity of the grafts were noted during the period of observation. The immunologic response evoked by a fresh corneal graft as compared to that of a preserved corneal graft was noteworthy. The comparative observations of the immunologic donor-recipient reactions and the clarity of the fresh and preserved lamellar heterograft made immediately after the operation and during the nine to 14 weeks of postoperative treatment are summarized in the following paragraphs.

* Neosporin®, Burroughs Wellcome and Company, Inc., Tuckahoe, New York.

†Metreton®, Schering Corporation, Bloomfield, New Jersey.

‡ Cyclogel®, Schieffelin and Company, New York, New York.

‖ Neo-Delta Cortef®, The Upjohn Company, Kalamazoo, Michigan.

Observation of immunologic response and clarity of grafts

Group 1. This group included recipient eyes that responded with a 0 to 1 plus reaction. Minimal reaction was noted in the eyes with preserved grafts, and a mild reaction occurred in those receiving fresh tissues. Conjunctival congestion was slight. There was mild superficial edema of the graft and surrounding one mm. of recipient cornea, and a minimum of neovascularization around the graft which disappeared following the removal of the sutures. The anterior chambers remained clear, the pupils round, and the iris reaction was normal. In one instance, the preserved human graft appeared clear from the beginning. In a second and third it became clear following the removal of the corneal sutures on the 10th day. The remaining preserved and fresh grafts of human, horse, monkey, cat and dog gradually cleared in one to three weeks. The intensity of reaction, however, was less with the preserved grafts than it was with fresh grafts.

Group 2. These recipient eyes reacted moderately to the donor grafts and were graded as 2 plus. The inflammatory signs in the preserved grafts were less than those noted in the fresh grafts. There was moderate ciliary injection, mild superficial edema of the graft with temporary clouding of the recipient corneas for a distance of two mm. and an inflammatory type of fine neovascularization surrounding the peripheral area of the graft and recipient cornea. There was questionable iritis and constriction of the pupil which disappeared following the use of cyclopentolate hydrochloride. The reactions were less intense when a preserved donor cornea (human, horse, monkey, cat and dog) was used than when a fresh donor cornea was used. The reaction was moderate in the group receiving fresh corneal tissue, but this subsided gradually and the graft cleared. In this group, complete transparency of the graft occurred within three to five weeks after operation.

Group 3. The recipient eyes in this group reacted in a more severe manner and these were graded as 3 to 4 plus. The reaction was more violent when fresh grafts were used than when preserved tissues were used. These animals showed edema of the eyelids, conjunctival chemosis, and permanent opacification of the graft with clouding of the surrounding three mm. of recipient cornea. There was neovascularization throughout the base of the graft. Iritis was moderate to severe with hazy anterior chambers and constricted pupils. At the end of 12 to 14 weeks patches of clarity appeared in the center, leaving a partly opaque graft. After 12 weeks there was a dense ring of cicatrization around the grafts, and in the remaining worst cases of this group (human, horse, monkey, cat and dog grafts) the end-result was complete opacification.

Over-all tolerance of lamellar heterografts revealed that the antigen-antibody type of reactions occurred in all tissues but were less frequent with preserved corneas than with fresh corneas. The human corneas caused fewer reactions than those seen with either horse or monkey corneas. Reactions with the use of cat corneas occurred less frequently than those with dog corneas.

A comparative analysis of the incidence of graded severity of immunologic response in the above classified groups of fresh and preserved lamellar heterografts was recorded and all the animals were killed at the end of nine to 14 weeks following operation. The recipient eyes were enucleated, the histopathologic studies were done, and the results were compared with the above findings (tables 2 and 3).

Results

In Group 1, the early appearance was dramatic in that the one graft appeared transparent from the beginning. In this case the donor material was a preserved human cornea and the recipient animal was a cat (fig. 1). In the remaining grafts in this group there was minimal to mild reaction, as in the cases of fresh and preserved human, horse, monkey, and dog corneas to cats and cat corneas to dogs. In these, all the grafts were transparent in one to three weeks. In most of the cases the fresh and preserved grafts were slightly cloudy at first, then cleared gradually in a period of six or seven days as the epithelium from the host covered the graft. By the end of the second to third week the grafts reached their final transparency.

Fig. 1 (Chavan and King). Clear lamellar heterograft (preserved human to cat) six weeks following transplanatation. Donor cornea was preserved by dehydration in glycerine and stored in vacuum at room temperature for one year and 11 months.

In Group 2, some grafts cleared in three weeks and others in five. In Group 3, some were still partly opaque after 12 weeks, and others remained opaque from the beginning to the end of the experiments (figs. 2 and 3). This may have been due to severe edema, neovascularization at the base of the graft, and iritis.

The microscopic appearance of the hematoxylin-eosin stained sections showed an almost normal cornea in most of the sections of the successful grafts (preserved more than the fresh). The degree of cellular response, the edema of the graft and sur-

TABLE 2

COMPARATIVE ANALYSIS OF IMMUNOLOGIC DONOR-RECIPIENT REACTIONS AND CLARITY OF FRESH AND PRESERVED LAMELLAR HETEROGRAFTS

(Gross, slitlamp, and microscopic appearance)

Gross and Slitlamp Appearance: Classified Groups, Profiles and Features of Immunologic Response	Graded Severity of Response		Number of Donor Grafts										Graft Status and Clearing Time after Local Therapy	Histopathologic Findings	Final Results
			Human		Horse		Monkey		Cat		Dog				
	F	P	F	P	F	P	F	P	F	P	P	P	F and P	F and P	F and P
Group 1															
a. Clear from beginning	0	0	0	1	0	0	0	0	0	0	0	0	Clear from beginning	Completely transparent cornea, no cellular response, except minimal hyperplasia of epithelium. Parallel arrangement of stromal fibers. It was difficult to distinguish the demarcation line between donor and recipient tissues	Excellent
b. Conjunctival congestion and superficial corneal edema	1+	0+	1	2	2	3	2	3	1	2	1	1	Clear in 1 to 3 weeks	Transparent corneas, except for mild hyperplasia of epithelium, without cellular response. Donor tissues appeared somewhat more intensively stained than recipient tissues	Good
Group 2															
a. Superficial corneal edema and neovascularization surrounding peripheral area of the graft and recipient cornea	2+	1+	3	2	1	1	1	1	1	1	0	1	Gradually clear in 3 to 5 wk.	Clear corneas, except line between donor and recipient tissues was seen as a zone of increased density with fixed nuclei of corneal corpuscles or keratoblast and moderate hyperplasia of epithelium	Fair
Group 3															
a. Deep corneal edema, neovascularization at base of graft and surrounding recipient cornea	3+	2+	3	3	3	3	3	2	4	3	4	3	Partly opaque in 12 to 14 wk.	Moderate hyperplasia of epithelium, irregular pattern of stromal fibers with keratoblast, translucent cornea in the center and fibroplastic opaque dense cicatrization line at the periphery of graft and surrounding the recipient cornea with moderate to severe neovascularization at base of graft	Poor
b. Deep corneal edema, opacification, neovascularization at base of graft and surrounding recipient cornea, and iritis	4+	3+	2	1	3	2	3	3	3	3	4	4	Completely opaque from beginning	Marked hyperplasia of epithelium forming epithelial facets at the margins of the graft, minimal to moderate loss of stromal elements with foreign body reaction, keratoblast, fibroblast with marked scarring, neovascularization at base of graft, and iritis. In these, lymphocytes were the predominant infiltrating cells rather than eosinophiles or polymorphonuclear leukocytes	Failure

F = fresh; P = preserved, 0 = absent; 0+ = minimal; 1+ = mild; 2+ = moderate; 3+ = severe; 4+ = worst.

rounding cornea, the neovascularization, opacification, and iritis were not observed in Groups 1 and 2, except for minimal to mild hyperplasia of the epithelium.

In Groups 1 and 2, most of the fresh and preserved grafts the stromal fibers in the grafted area appeared in a regular pattern of parallel arrangement. The nuclei of the corneal corpuscles varied from large, dark staining ones to those which were thin and pale, but they were distributed equally in the stromal fibers. A few striking examples of successful fresh and preserved human to cat, horse to cat, monkey to cat, cat to dog, and dog to cat transplants, respectively, resulted in such perfect and fully transparent corneas that when seen under microscopic sections it was difficult to find the line between the

TABLE 3

COMPARATIVE ANALYSIS OF INCIDENCE OF GRADED SEVERITY OF IMMUNOLOGIC REACTIONS OF FRESH AND PRESERVED LAMELLAR HETEROGRAFTS*

Graded Severity of Response		Donor Tissues									
		Human Grafts		Horse Grafts		Monkey Grafts		Cat Grafts		Dog Grafts	
		F	P	F	P	F	P	F	P	F	P
Group 1											
Zero	(0)	0	1	0	0	0	0	0	0	0	0
Minimal	(0+)	0	2	0	3	0	3	0	2	0	1
Mild	(1+)	1	2	2	1	2	1	1	1	1	1
Group 2											
Moderate	(2+)	3	3	1	3	1	2	1	3	0	3
Group 3											
Severe	(3+)	3	1	3	2	3	3	4	3	4	4
Worst	(4+)	2	0	3	0	3	0	3	0	4	0
TOTAL GRAFTS		9	9	9	9	9	9	9	9	9	9

* Based upon gross and microscopic findings (Table 2).
F = fresh; P = preserved.

donor and recipient tissues (fig. 4.) Other sections of preserved grafts (dog and cat) clearly showed a difference in staining. The donor tissues appeared more intensively stained than the tissues of the recipients.

In Group 3, most of the fresh and preserved grafts became partly opaque. A dense line of cicatrization was found at the periphery of the grafts which involved the surrounding two to three mm. area of recipient tissue. There was also moderate to severe type of hyperplasia of the epithelium, irregular pattern of the stromal fibers with keratoblasts, fibroblasts, severe type of neovascularization at the base of the graft, iritis and complete opacification of the grafts. In these, lymphocytes rather than eosinophiles or polymorphonuclear leukocytes were the predominant infiltrating cells.

The preserved corneas used had been stored from four months to two and one-half years. The graft age after transplantation was nine to 14 weeks, and most of the grafts remained clear during the observation

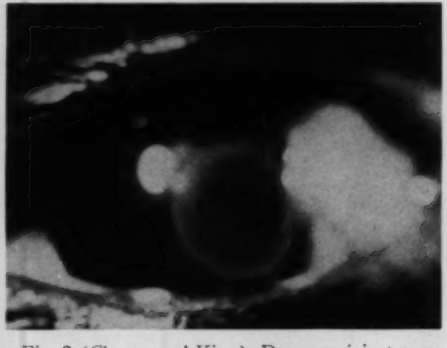

Fig. 2 (Chavan and King). Donor-recipient reaction forming a ring of cicatrization round the partly opaque lamellar heterograft (preserved dog to cat) 12 weeks following transplantation. Donor cornea was preserved by dehydration in glycerine and stored in vacuum at room temperature for two years and six months.

Fig. 3 (Chavan and King). Complete opacification of the lamellar heterograft (fresh dog to cat) following six days of violent donor-recipient reaction. Donor graft remained permanently opaque from the beginning to the end of 14 weeks of local therapy.

period (tables 1 and 2). The fate of lamellar heterogenous grafts of fresh and preserved corneas, both grossly and histopathologically as compared and judged by the percentage of the clear and unclear grafts, is indicated in Tables 4 and 5.

Comment

Successful results in lamellar heterografting are difficult to obtain. The tissue of the donor and the recipient have neither the same thickness nor the same curvature. This difficulty can be minimized by special care in operating technique. There is considerable difference in biologic constitution which may produce an antigen-antibody type of reaction.

In our experiments with fresh and preserved grafts, however, some favorable results were obtained. The postoperative treatment employed seemed to be effective in lessening the immunologic response in the three groups classified above. This was especially effective in suppressing the five features resulting from donor-recipient reaction—conjunctival congestion, corneal edema, neovascularization, corneal opacification, and iritis—and in promoting rapid clearing of the grafts in Groups 1 and 2.

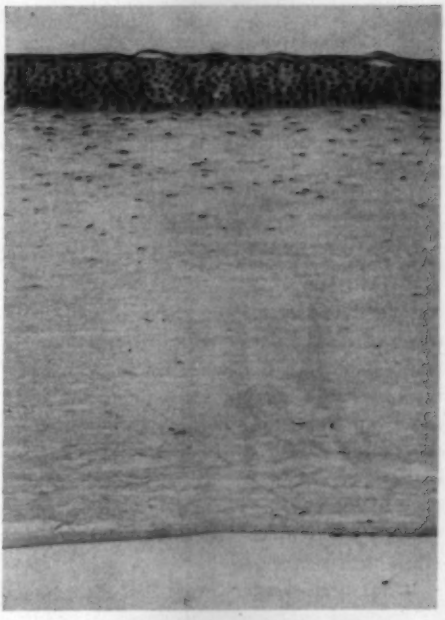

Fig. 4 (Chavan and King). Clear section through the area of lamellar heterograft (preserved human to cat) following nine weeks of local therapy. Donor cornea was preserved by dehydration in glycerine and stored in vacuum at room temperature for one year and 11 months.

In Group 3, however, most of the grafts remained partly opaque and some remained

TABLE 4

COMPARATIVE ANALYSIS OF FATE OF FRESH AND PRESERVED LAMELLAR HETEROGRAFTS*

(Percentage)

Final Results	Donor Tissues										Average Difference Between Fresh and Preserved Grafts
	Human Grafts		Horse Grafts		Monkey Grafts		Cat Grafts		Dog Grafts		
	F	P	F	P	F	P	F	P	F	P	
Successful grafts											
1. Excellent	0	11	0	0	0	0	0	0	0	0	
2. Good	11	22	22	33	22	33	11	22	11	11	
3. Fair	33	22	11	11	11	11	11	11	0	11	
Average	44	55	33	44	33	44	22	33	11	22	11
Unsuccessful grafts											
4. Poor	33	33	33	33	33	22	44	33	44	33	
5. Failure	22	11	33	22	33	33	33	33	44	44	
Average	55	44	66	55	66	55	77	66	88	77	11

* Based upon gross and microscopic final results (table 2).
F = fresh; P = preserved.

TABLE 5

COMPARATIVE ANALYSIS OF TOTAL RESULTS OF SURGICALLY SUCCESSFUL AND UNSUCCESSFUL GROUPS OF FRESH AND PRESERVED LAMELLAR HETEROGRAFTS*

(Total percentage)

Average Graft Status	Fresh Groups	Preserved Groups	Difference Between Fresh and Preserved Groups
1. Successful grafts	28.6	39.6	11
2. Unsuccessful grafts	70.4	59.4	11

* Based upon the average percentage of successful and unsuccessful groups of fresh and preserved lamellar grafts (table 4).

completely opaque from the beginning, because of severe donor-recipient reactions. It was also obvious that when the inflammatory response was slight, wound healing was more rapid and the tolerance by the host of the donor grafts was better and led to a higher percentage of success and transparency of the grafts. These factors were more evident when preserved tissues rather than fresh grafts were used.

It has been demonstrated that the process of freeze-drying and subsequent reconstitution and extraction in water or physiologic saline removed some of the protein from nonviable arterial grafts.[12] The precipitin tests in rabbits suggest that some of the antigenic properties are also removed.[12] It is quite possible that these two phenomena might be related to the corneas preserved by the similar process of dehydration in glycerine and subsequent reconstitution in saline-antibiotic solution. These may be the factors in the lessening of immunologic donor-recipient reactions or antigen-antibody response noticed in clinical and histopathologic studies of this experiment. The scarring, neovascularization, and fibroblastic response was observed less in preserved grafts than in fresh grafts. It is also probable that the toxic effects produced by the "heteroproteins" resulting from tissue incompatibility may be due to the difference in the biologic constitution of the corneal tissues which may have been altered by a high concentration (95 percent) of glycerine preservation.

Payrau and his associates[13] reported the successful utilization of corneas preserved by lyophilization (freeze-drying) in homografts and heterografts. They found that the donor corneas were nonviable but were not altered in physical structure. Lamellar heterografts from dog to man seemed to do well, but similar grafts from pig to man did very poorly. These research workers do not advise the use of heterografts, but they feel that their technique of lyophilization makes homografts and heterografts more alike.

In comparing the results of these authors[13] with our work on corneas preserved by dehydration in glycerine for lamellar homografts[2-4] and heterografts of this experiment, we found some similarity; tissue culture studies also showed nonviable tissues in 100 percent of the specimens reported by several authors[14,15] and their findings are also confirmed by our recent tissue culture studies.[16] However, in our findings the use of preserved dog corneas in cats resulted in a more severe degree of immunologic donor-recipient reaction than any other tissues used in this experiment. Whether or not preserved dog corneas used in human beings will be less antigenic and the results will be similar to those with fresh or preserved lamellar type of human homografts is still not determined.

In microscopic sections of fresh and preserved grafts of different species, no variations were found, and their structures were similar. The lamellar heterografts of preserved tissues seem to have a better chance of clearing with fewer types of antigen-antibody reactions than those with fresh tissues.

Summary and Conclusions

1. Experimental lamellar heterografts utilizing corneas preserved by dehydration in glycerine have been compared with fresh lamellar heterografts.

2. Five types of profiles and features of immunologic donor-recipient reactions and clarity of the grafts have been observed in the three classified groups of the experimental animals and the results have been compared with histopathologic findings.

3. Over-all tolerance of lamellar heterografts revealed that the antigen-antibody types of reactions which occurred with all donor tissues were less frequent with preserved corneas than with fresh corneas.

4. The human corneas resulted in fewer antigen-antibody reactions than those seen with either horse or monkey corneas. Antigen-antibody reactions with the use of cat corneas occurred less frequently than those observed with dog corneas.

5. In regard to the fate of lamellar heterografts, the two opposing theories of regeneration versus retention are supported by the results of this experiment.

Georgetown University
Medical Center (7).

Neosporin® Ophthalmic Solution used for this study was supplied through the courtesy of Dr. E. N. Whitman of Burroughs Wellcome & Company, Tuckahoe, NewYork. We are indebted to Dr. H. V. Pifer, Jr., Clinical Research Division, Schering Corporation, Bloomfield, New Jersey for the generous supply of Metreton® used in this experiment.

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CLINICAL EFFECTS OF NEPTAZANE*

FUMIO KANDORI, M.D., YOSHITOSHI KUROSE, M.D., AND SHINJI KURIMOTO, M.D.
Tottori, Japan

Neptazane (5-acetylimino-4-methyl = Δ^{2}-1, -3, 4-thiadiazoline-2-sulfonamide) is a new carbonic anhydrase inhibitor. Recently, Becker[1] (1957) and Langham[2] (1958) reported that Neptazane is more effective than the well-known Diamox in reducing the intraocular pressure and the rate of formation of the aqueous humor. There are as yet only a few reports on this effective drug for glaucoma.

Our objective is to evaluate clinically the value of Neptazane in decreasing intraocular pressure and to investigate its side-effects.

MATERALS AND METHODS

Five normal subjects and 10 patients with glaucoma were investigated. The latter were divided into "active," in which the intraocular pressure was over 35 mm. Hg (seven eyes), and "quiescent" in which the tension was under 35 mm. Hg (eight eyes) on admission.

Each subject was hospitalized and examined at the Kandori Ophthalmological Institute of Tottori University Hospital.

In the present series of experiments, 100 mg. Neptazane were orally administered twice daily for three days (generally, at intervals of 12 hours) but only once in the morning on the third day.

Tonometry and tonography were taken with a standard Schiøtz tonometer and Friedenwald's table of 1955 and Grant's formula were used to calculate the ocular tension (mm. Hg), the facility of outflow (cu. mm./min./mm. Hg = C-value) and the rate of flow (cu. mm./min. = F value).

Serum sodium and potassium, before and after the administration of 500 mg. Neptazane, were estimated by the flame photometer and during these measurements the patient was allowed routine meals at the hospital but the water intake was controlled.

The urinary pH and blood pressure were measured occasionally.

RESULTS

1. OCULAR TENSION

Two typical responses of the ocular tension to 100 mg. Neptazane twice a day for three days are given in Figure 1. These curves in Figure 1 show that the variation in the ocular tension after Neptazane differed in individuals or according to time of administration. However, it showed considerable uniformity in both eyes of an individual.

The general effect of Neptazane on the intraocular pressure is summarized in Figure 2. Each point in Curves A, B, and C represents the average ocular tensions of normal, quiescent, and active glaucomatous eyes for every 100 mg. Neptazane given orally, while the average variation of maximum fall in ocular tension is shown in Curves a, b, and c. The maximum fall in tension in active glaucoma was greater on the degree than in the other groups; in all groups, the largest maximum fall followed the first dose of 100 mg. Neptazane. After total dosages of 500 mg. the average ocular tension fell in all groups, especially in the active glaucoma group; however, with this dosage of Neptazane no effects were observed on the ocular tension in seven of 15 normal eyes and two of seven eyes with active glaucoma.

After 100 mg. Neptazane orally, control of tension began in 30 minutes to two hours and continued for over 10 hours in 71 out of 93 eyes investigated. In 14 of 73 in the normal group, six of 36 in the quiescent glaucoma group, and six of 29 in the active glaucoma group there was no fall in tension.

2. TONOGRAPHIC FINDINGS

Table 1 shows the facility of outflow (C

* From the Department of Ophthalmology, Tottori University, School of Medicine.

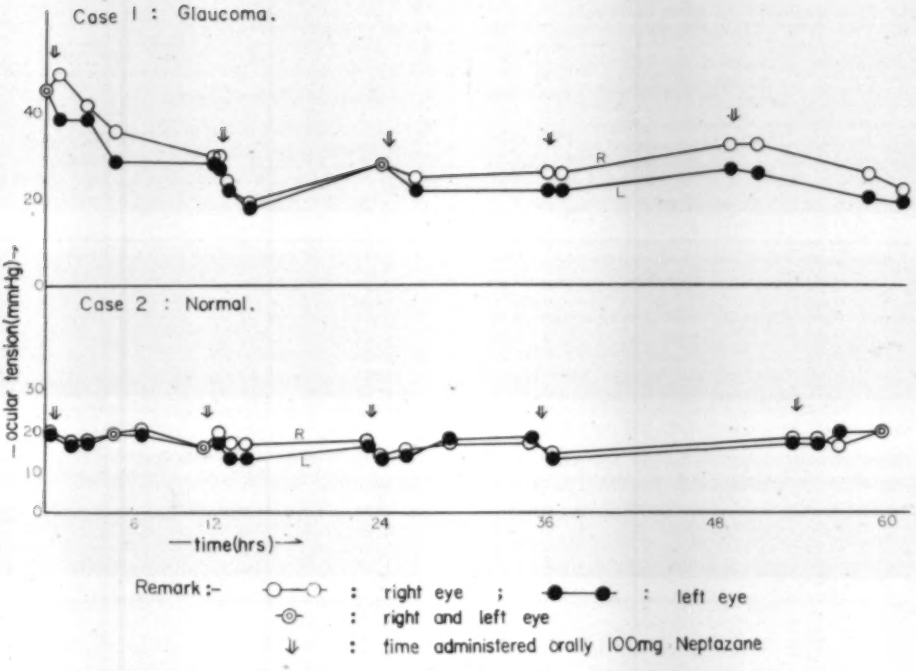
Case 1 : Glaucoma.
Case 2 : Normal.
— ocular tension(mmHg) →
— time(hrs) →
R
L
Remark :- : right eye ; : left eye
: right and left eye
: time administered orally 100mg Neptazane

Fig. 1 (Kandori, et al.). Two typical responses of the ocular tension to Neptazane (100 mg. twice daily for three days).

value) and the rate of flow (F value) before and two hours after oral administration of 100 mg. Neptazane. The change in C value, without regard to the normal and glaucomatous eyes, before and after 100 mg. Neptazane is not significant ($t_s = 0.0269 < 0.13 = t_{28}^{0.90}$), while the change in F value is reasonably significant ($t_s = 2.01 > 1.73 = t_{28}^{0.10}$); that is, F value decreases after Neptazane uptake.

3. Side-effects

1. Subjective symptoms. At a therapeutic dosage of Neptazane, the only complaints were slight gastro-urinary and gastro-intestinal ones in a few patients.

2. Serum potassium and sodium. Serum

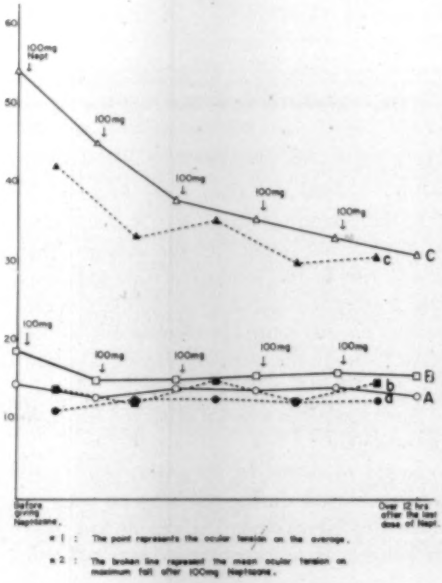

Fig. 2 (Kandori, et al.). Effect of Neptazane on the ocular tension of a normal eye (A,a), an eye with quiescent glaucoma (B,b) and an eye with active glaucoma (C,c).

TABLE 1

EFFECT OF 100 MG. NEPTAZANE TAKEN ORALLY ON TONOGRAPHIC VALUE OF NORMAL AND GLAUCOMATOUS EYES

Facility of Outflow*			Rate of Flow†		
Before Giving Neptazane	Two Hours after Neptazane	Difference	Before Giving Neptazane	Two Hours after Neptazane	Difference
		I. Normal Group			
0.39	0.39	0	0.39	0.39	0
0.37	0.45	−0.08	1.29	1.12	0.17
0.31	0.30	0.01	2.17	1.50	0.67
0.26	0.19	0.07	0.53	0.38	0.15
0.34	0.26	0.08	2.04	0.79	1.25
0.30	0.38	−0.08	1.50	1.92	−0.42
0.45	0.50	−0.05	4.55	4.50	0.05
0.49	0.54	−0.05	4.45	4.86	−0.41
0.24	0.25	−0.01	0.96	0.63	0.33
0.29	0.40	−0.11	2.03	2.40	−0.37
0.50	0.25	0.25	4.54	1.25	3.29
0.22	0.20	0.02	1.57	0.80	0.77
0.25	0.27	−0.02	1.25	1.35	−0.10
0.28	0.31	−0.03	1.96	0.78	1.18
		II. Glaucoma Group			
0.08	0.06	0.02	1.44	0.84	0.60
0.03	0.03	0	0.36	0.33	0.03
0.29	0.28	0.01	2.32	1.96	0.36
0.47	0.52	−0.05	4.23	4.16	0.07
0.43	0.36	0.07	3.91	3.24	0.67
0.33	0.33	0	4.95	4.29	0.66
0.11	0.08	0.03	1.98	1.76	0.22
0.08	0.10	−0.02	1.76	2.00	−0.24
0.03	0.03	0	1.11	1.29	−0.18
0.21	0.27	−0.06	2.73	3.24	−0.51
0.18	0.29	−0.11	1.29	3.19	−1.90
0.03	0.01	0.02	1.41	0.55	0.86
0.23	0.19	0.04	1.64	0.47	1.17
0.21	0.19	0.02	0.64	0.47	0.17
0.02	0	0.02	0.70	0	0.70

* The difference between the facility of outflow before and after giving 100 mg. Neptazane:
$t_0 = 0.0269 < 0.13 = t_{25}^{0.90}$

† The difference between the rate of flow before and after giving 100 mg. Neptazane orally:
$t_0 = 2.01 > 1.73 = t_{25}^{0.10}$

sodium before and after total doses of 500 mg. Neptazane (table 2) was, in most cases, within normal range. On the average, there was a rise in the level of serum sodium 20 hours after the last dose of 100 mg. Neptazane. This was more apparent in normal subjects than in the patients having glaucoma ($F_{24}^{3} = 17.016 > 5.519 = 2F_{24}^{3(0.005)}$).

Such a relation was not observed for serum potassium.

3. pH of urine. In six cases, urinary pH was measured during the day of administration of Neptazane. The results are shown in Table 3. In all cases the urinary pH had a tendency to alkalinize following Neptazane administration; this ceased within 20 hours after withdrawal of the drug.

4. Blood pressure. No correlation between blood pressure and intraocular pressure was noticed in this experiment.

COMMENT

The clinical finding that carbonic anhydrase inhibitors are effective in lowering intraocular pressure in humans was first reported by Becker.[3] Since then many clinical investigations of the effect of carbonic anhydrase inhibitors on the formation of aqueous

humor and the decrease of ocular tension have been carried out with this drug.

Clinically, though it is established that Diamox is a useful and helpful drug for glaucoma, there is room for improvement in the availability, efficacy, and long-term effects.

Neptazane is a new carbonic anhydrase inhibitor having the following chemical structure as compared to Diamox:

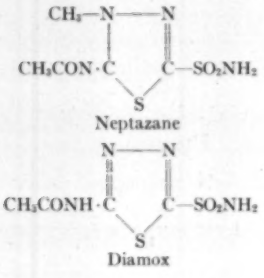

TABLE 2

EFFECT OF 500 MG. NEPTAZANE* ON SODIUM AND POTASSIUM IN SERUM

Subject No.	Sodium†		Potassium	
	Before Neptazane	After Neptazane	Before Neptazane	After Neptazane
	I. Normal Group			
1	140.8	158.3	4.1	4.7
2	139.8	157.6	5.0	4.0
3	139.8	150.0	4.4	4.4
4	139.8	153.9	4.4	4.6
5	136.6	146.1	4.6	4.1
TOTAL	596.8	765.9	22.5	21.8
	II. Glaucoma Group			
6	142.8	156.2	4.3	4.5
7	149.0	146.9	3.7	6.5
8	140.8	154.1	3.8	4.6
9	138.4	148.9	4.1	4.1
10	142.0	149.0	4.4	3.5
11	138.0	150.0	4.2	5.1
12	142.8	146.0	4.1	3.8
13	146.1	154.3	4.1	3.2
14	148.5	150.0	4.5	5.0
TOTAL	1,288.4	1,355.4	37.2	40.3

* Neptazane was given five times at about 12-hr. periods (100 mg. orally).

† The average variation of sodium in serum was more apparent in normal subjects than in glaucoma patients.

$(F_{24}^{3} = 17.016 > 5.519 = F_{24}^{3(0.005)})$

TABLE 3

CHANGES IN pH OF URINE

Before Neptazane	After Neptazane	After 400 mg. Neptazane	One Day after Last Dose of Neptazane
5.2	6.6	7.0	5.4
5.6	5.6	6.8	5.8
5.4	5.4	7.0	5.4
5.6	5.6	6.6	5.6
5.6	6.4	6.6	5.8
6.2	7.2	—	6.0

Neptazane has an in vitro potency of about 1.3 to 1.6 times that of Diamox.[4] Becker[1] has reported that Neptazane was found, in rabbits and in patients, to lower intraocular pressure when administered in doses approximately one third to one fifth those of acetazolamide.

There are as yet few clinical reports on Neptazane. Langham[2] reported that a fall in the intraocular pressure in normal subjects and glaucoma patients was observed within one to two hours after 250 or 125 mg. Neptazane; the decrease remained for more than 18 hours after the last dose.

Our experimental results, giving 100 mg. Neptazane twice daily for three days (total dosage 500 mg.) showed that intraocular pressure began to fall in 30 minutes to two hours, at the latest, and was controlled for 10 hours in 71 out of 93 eyes measured. After total doses of 500 mg. of Neptazane, the decrease in ocular tension was noted in all groups, most especially in the active glaucoma group.

From these results, it seems safe to say that Neptazane is a more helpful and useful drug in lowering the ocular tension for glaucoma patients than Diamox.

The tonographic findings of Becker and Constant[5] and Kageyama[6] showed that systemic carbonic anhydrase inhibitors suppressed aqueous secretion in rabbit eyes. Our findings with Neptazane coincided with these reports.

Side-effects of this drug were reported by Langham; only one of his nine patients experienced a tingling sensation in hands

and feet. In our series, side-effects were subjectively minor for there were only slight gastrourinary and gastrointestinal complaints in two of 15 cases.

Serum sodium and potassium before and after oral administration of Neptazane (500 mg.) was investigated from two points of view—side-effects and in light of Friedenwald's[7] theory (1949) of relation between the intraocular pressure and the formation of the intraocular fluid, and of the report by Breinin and Grötz[8] that carbonic anhydrase inhibitors controlled aqueous humor secretion.

The report on the correlation between the systemic and intraocular effects of Diamox by Campbell and others[9] is interesting. They reported that serum sodium, especially in glaucoma patients, was below its original level for a certain period after administration of Diamox. On the other hand Kuwabara, et al[10] reported that serum sodium rose day by day during administration. With regard to serum potassium, carbonic anhydrase inhibitors decreased it (Campbell,[9] Kuwabara,[10] and Takaoka[11]).

In our studies, though the serum sodium before and after a total dose of 500 mg. of Neptazane varied in most cases, there was an increase 20 hours after the last dose of Neptazane. Generally speaking, it is expected that the electrolytes in serum vary with the administration of Neptazane, as is the case with Diamox. Furthermore, it is interesting to note that the increase of serum sodium of normal subjects after Neptazane was greater than in glaucoma patients.

The urinary pH during administration of Neptazane tended to alkalinize, but recovered to the initial pH 20 hours after the last dose. It is said that the alkaline tendency in urine pH after some carbonic anhydrase inhibitors is due to damage to the formation of H^+ on the epithelium of uriniferous tubules. Perhaps this also holds true for Neptazane.

Summary

A new carbonic anhydrase inhibitor, Neptazane, was clinically investigated—100 mg. were given twice daily for three days (total dosage 500 mg.).

In this dosage, Neptazane was effective in lowering the ocular tension in the human being, especially in glaucoma patients, without noteworthy side-effects.

Preliminary tonographic studies and studies of the electrolytes in serum before and after oral Neptazane, seem to indicate that this new carbonic anhydrase inhibitor has ocular and systemic effects similar to those of the well-known Diamox.

Department of Ophthalmology.

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NOTES, CASES, INSTRUMENTS

A NONMAGNIFYING READING AID

R. F. LEINBACH,* M.D.
Charlotte, North Carolina

The device herein described is presented as a reading aid which will be found helpful to some cataractous individuals whose visual disabilities are featured chiefly, for a time at least, by "haze" or "fog." In a fairly diligent investigation I have been unable to learn that a device of this character, or one employing the same principle, has been advanced at any time as a reading aid for individuals afflicted with cataract or other form of visual disability.

The device consists of a single sheet of jet black, lusterless Vinyl Rigid plastic, 1/32nd of an inch in thickness. (For purpose of trial, a sheet of jet black mat surface, lusterless paper may be cut to pattern.) For reading books and magazines of varying size, dimensions of the reading aid are: length nine inches; width four inches. Parallel to the long axis, and exactly midway between the long edges, is cut a perforating slit 0.25 inch in width, and approximately 7.25 inches in length. This slit extends to 0.25 inch of one short edge (to reveal letters nearest the binding) but only to 1.25 inches of the other short edge.

In use the reading aid is placed flatly on the page of print to be read. For prolonged reading it is most convenient to sit at a desk or table with book or journal lying flat on the table before one. Illumination for this position, in my experience, is most satisfactory when derived from a 100-watt or 150-watt Edison bulb, 18 or 20 inches above the table in a well-shaded table lamp placed just beyond the book and in front of the reader. The table should not be cluttered with highly reflective white papers.

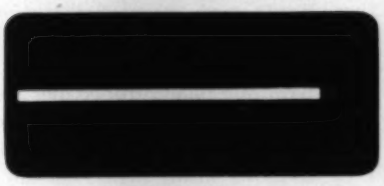

Fig. 1 (Leinbach). The reading aid.

Without resort to the reading aid, the cataractous person who may anticipate being helped by its use is immediately conscious that the printed page in front of him is impartially covered by the same haze which enshrouds his entire world. Since cataractous haze is a peculiar subjective perceptual experience it cannot be accurately quantitated, nor can it be reproduced by or for those not afflicted with the disease. As used here, the term indicates a condition similar to that experienced by a normal person on a mildly foggy morning when objects though visible are not sharply defined, contrast is diminished, and range of vision shortened by condensed atmospheric moisture. On cloudy days haze for the cataractous person is reduced, on bright sunny days at its maximum. The term "glare" sometimes used is by definition wholly inappropriate.

A characteristic effect of cataractous haze on printed matter is that contrast between black lettering and white paper is greatly diminished. Printer's ink appears gray and pallid, fading more and more as lenticular degeneration advances. Words, though still distinguishable as such and as short, medium, or long, are illegible or read only by the closest scrutiny depending on size of type. If a reading glass is now used, letters are magnified and become legible. It is noteworthy, however, that the element of haze has not been dissipated in any degree.

The nonmagnifying reading aid is now placed flatly on the page. One or two lines of print are visible through the exposure slit. Ten or more lines above and below are

* An internist retired by cataract.

covered for the moment, those below to be progressively uncovered in the process of reading. It can now be noted that letters and words appearing in the exposure slit are no longer covered with haze. Contrast between type and white paper has been notably increased. Printer's ink has regained its normal blackness. Letters are now clearly defined, rendering words easily distinguishable. This return of contrast should restore to readability print one or two sizes smaller than was previously considered within one's capabilities. In my case, whereas 8-point type (newspaper "body" type) is illegible in diffuse daylight, 7-point, 6-point, and 5-point type can be fluently read by use of the reading aid and properly placed illumination.

Why should a simple device of this character exert such a marked influence in dispelling haze for which an irreversible lenticular degeneration is responsible? Much light on this question is derived from the observable fact that if there is placed before a victim of cataractous haze a page of type printed from a reversing plate, yielding white lettering on an all black background, it will be noted by him that over this page of print there is no haze. It then becomes apparent that there is an extraocular and external factor of great influence in the production of haze. This external factor may reasonably be assumed to be the reflection of light rays falling on unprinted areas of white paper around the margins of boxed type, between lines, between letters, and within letters.

If this assumption is correct, it becomes obvious that the virtue of this nonmagnifying reading aid resides in its broad nonreflective upper and lower flanges which intercept by calculation 95 percent of the light rays falling on its coverage area. The reading aid is thus seen to be a method of providing a movable black background for the universal black lettering on white paper.

It is not to be supposed that this reading aid is advanced as a means of escaping or postponing operation. It is presented entirely as a method of reading, by which an individual of studious habits, for whom operation may have been necessarily or advisedly postponed, may be able to continue his former habits of prolonged reading without the ceaseless annoyance of haze and without the wearisome necessity of poising, focussing and shifting a reading glass, a method of reading usually abandoned at the earliest possible moment.

It must be noted also, that in perusing areas other than linear, as in the study of maps, charts, diagrams, graphs, musical scores, photographs, and generally in the inspection of material objects, a reading glass is far superior in spite of its continuing haze. Likewise for brief reading, as in searching city and telephone directories, consulting dictionaries and tables, a reading glass is generally more suitable.

In the following paragraphs, transcribed from a letter* received since this paper was written, appears an analysis of intraocular events as influenced by this reading aid.

In cataract the swelling of the lens and the reduction of its transparency reduces the amount of focal light which reaches the retinal image of the object of regard. On the other hand, these same factors increase the amount of nonfocal light scattered over the retina. This latter causes a reduction in contrast—and therefore in visibility—of the object of regard. At the same time, the ambient light helps to constrict the pupil—which in turn also reduces visibility of the object of regard—by reducing the retinal illumance of the focal light at the fovea and by ob-

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* Personal communication, July 24, 1959, from Mathew Alpern, Ph.D., Department of Ophthalmology, University of Michigan Medical School, Ann Arbor, Michigan.

For local production, the plastic material may be obtained from the Commercial Plastics and Supply Company, 630 Broadway, New York 12, in sheets 21 by 50 inches, specifying Vinyl Rigid, 1/32 of an inch, jet black, mat surface, lusterless. Any printing house able to cut printer's dies can cut the pattern.

If difficulty is encountered, the reading aid can be obtained for the present from Pound and Moore Company, 304 South Tryon Street, Charlotte 1, North Carolina, at $1.00 each by mail, postpaid.

Pocket size models, 6¾ by 3¼ inches in material 1/16th of an inch in thickness are also obtainable at the same price.

securing more transparent parts of the lens by the iris.

The reading aid described in this paper acts to reduce the amount of light scattered by the eye media by permitting only light in the immediate neighborhood of the object of regard to enter the eye. This therefore: (a) reduces the contrast reduction from ambient light and (b) dilates the pupil so that more transparent regions of the eye media allow more focal light to reach the fovea. Both of these factors improve the visibility of object of regard. Another way of doing essentially the same thing would be to use white letters on a black background.

2601 Sherwood Avenue (7).

RETINAL PHOTOGRAPHY AND OPHTHALMOSCOPY COMBINED IN ONE INSTRUMENT*

GERALDO QUEIROGA, M.D.
Belo Horizonte, Brazil

Photography of the retina is of great medical value not only for the ophthalmologist but also for medical science as a whole. Unfortunately the professional acceptance of this technique has been rather slow due to the rather high prices of the necessary equipment. Up to the present time the ophthalmologist has had to use several instruments for visual observation and for photography of the retina. I felt that an instrument combining both procedures would be much desired. Fortunately, the optical illumination system of both instruments is the same, both use the Gullstrand reflex-free system. The only difference is that in the instrument used for photography a camera is substituted for the eyepieces.

For several years (1942) I have been experimenting and found that the Bausch & Lomb binocular ophthalmoscope can be used for both procedures. Previous attempts have been made. In one, Edwards in 1952, used a 90-mm. objective (mounted on a tripod) in connection with the Bausch & Lomb binocular ophthalmoscope. As illumination, he used a 500-volt movie bulb.

During the war it was impossible to import the Nordensen Camera; therefore, I designed (1943) an adapter which would permit photoretinography by means of a Bausch & Lomb binocular ophthalmoscope and a single reflex camera (Exacta).

With the Exacta (Varex or Exa plus-a-tessar f.3.5 lens, and a penta prism, the technique was improved and color retinal pictures were attempted. Instead of having the camera attached to a tripod, a special bracket was made. Color pictures were taken overrunning the ophthalmoscope light bulb with a special electrical mechanical device. The reflex of the filament bulb in the aspheric lens was masked off by means of a black dot, according to van der Heydt.

In January, 1956, in order to improve the luminosity of the ophthalmoscope aspheric lens, I asked D. F. Vasconcelos, São Paulo, Brazil, to coat the lens. The pictures were very much improved and later (1957), Bausch & Lomb prepared two binocular ophthalmoscopes with black dots and coated aspheric lenses. This instrument and the photographic device were exhibited at the Pan-American meeting held in New York.

In the Bausch & Lomb binocular ophthalmoscope, the decentration of the illuminating system from the observation system through the pupil is accomplished in such a way that ophthalmoscopy is practically reflex free and rich in details, if two black dots are added to the coated aspheric objective. The light penetrates into the eye through an illuminating area, which is the image of the bulb's filament, in the lower edge of the pupillary area (fig. 1). This is essential for both good ophthalmoscopy and good photoretinography. Behind prism, P, a photographic camera or an ocular catch, the inverted and real image of the retina is formed on the ophthalmoscope tube.

TECHNIQUE

1. Remove the eyepiece system from the

* From the Faculdade de Ciencias Medicas, Catholic University of Minas Gerais, Brazil. Exhibited at meeting of the Pan-American Association of Ophthalmology, New York, April, 1957.

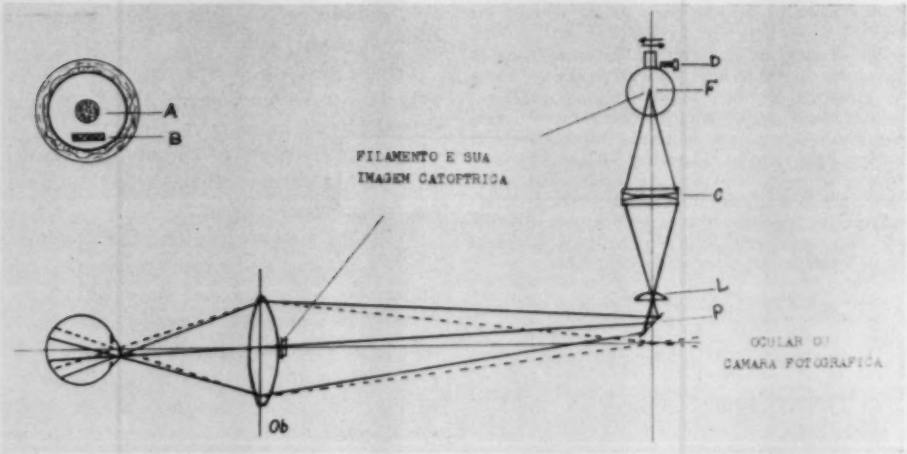

Fig. 1 (Queiroga). Gullstrand illuminating system. Illuminating system (B) and viewing system (A) in the pupil. (D) Adjusting screw. (F) Lamp filament. (C) Condenser. (L-P) Lens prism. (Ob) Aspheric objective.

Bausch & Lomb binocular ophthalmoscope and adjust a 35-mm. single-reflex camera (Exacta or Exa) to the ophthalmoscope tube by means of a camera bracket (fig. 2-A). This special support is essential in order to render the optical axis of the camera coaxial with the optical axis of the ophthalmoscope. The real and inverted image of the retina can be focused through the view-finder of this single reflex camera.

The camera has the following characteristics: single reflex camera, objective f. 3.5

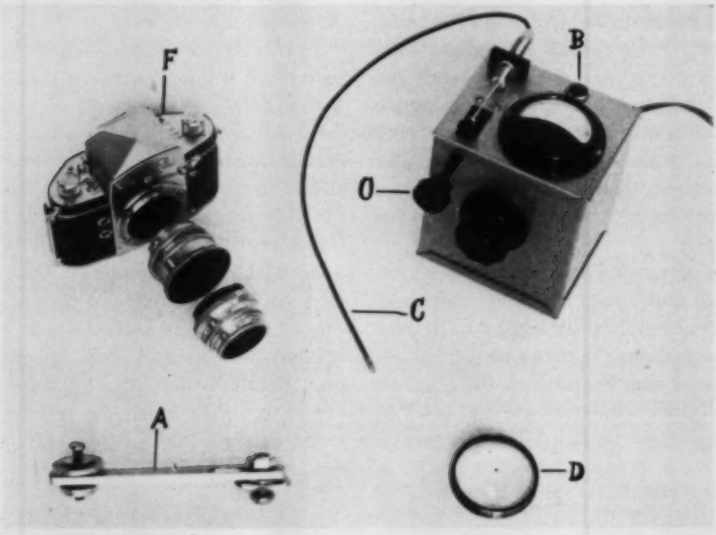

Fig. 2 (Queiroga). (A) Bracket to support the camera. (B) Electrical mechanical device. (O) Push button. (D) Aspheric lens with black dots. (F) Exa camera with extension tubes. (C) Cable release.

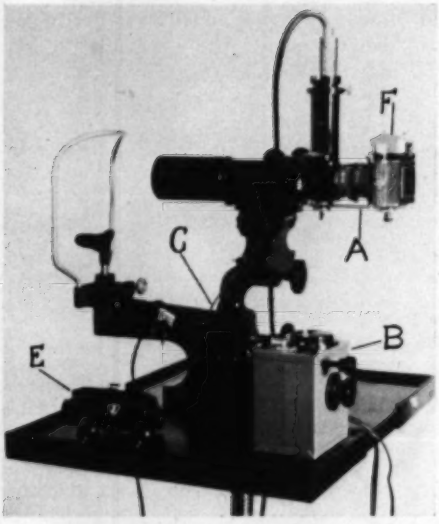

Fig. 3 (Queiroga). Bausch & Lomb binocular ophthalmoscope adapted to retinal photography. (E) Eyepiece. (F) Exa camera. (A) Bracket to support the camera. (B) Electrical mechanical device. (C) Cable release.

coated lens, with a focal length 50-mm.; to increase the focal length of the objective an extension tube is provided with a minus lens.

2. The image of the lamp filament in the front ophthalmoscope lens is eliminated by means of two dark dots. Adjusting screw D (fig. 1) makes this easy.

3. An electrical mechanical device (fig. 2-B), having a circuit normally connected with the same light source of the ophthalmoscope, permits low illumination for inspecting and focusing the retina and a flash for the snapshot. During the short time the ophthalmoscope lamp is brightly illuminated, the photographic film is exposed by means of a push-button (fig. 2) which controls the camera's shutter.

All the photographs are done under the same light intensity by means of a rotary type switch and volt meter. This electrical mechanical device provides an intense, narrow pencil of light, entering the eye close to the margin of the pupil. In this way a sufficient amount of light reaches the retina for photography. I have done about 450 color photographs using this technique. The average loss is about one retinal photograph in four. Presently, the exposure time is 1/25 of a second with super anscochrome. The area photographed includes the macula and optic disc. When doing panoramic photography of the retina the Wessely fixation device is attached to the instrument and is quite helpful.

In cases of high ametropia, the auxiliary lens slide, which is standard equipment of Bausch and Lomb's binocular ophthalmoscope, can be used the same way as in regular ophthalmoscopy (figs. 3 and 4).

With this technique the Bausch and Lomb binocular ophthalmoscope and a single reflex camera can be easily combined into one instrument, permitting the physician to visualize the retina through the ophthalmoscope and take retinal photographs as well. This pro-

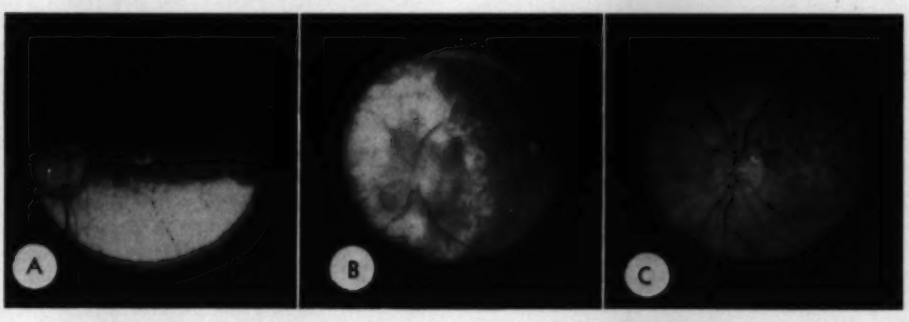

Fig. 4 (Queiroga). Retinal photographs. (A) Normal dog fundus. (B) Coats' retinitis. (C) Central choroidoretinal degeneration.

vides him comparatively simple and inexpensive permanent records of retinal conditions. The retinal photographs can either be viewed by means of a simple slide viewer or a standard slide projector.

Felipe dos Santos (382).

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PERIPHERAL MELANOBLASTOMA OF CHOROID*

(PARA) CENTRAL SCOTOMA AS AN INITIAL SIGN

C. KOK-VAN ALPHEN, M.D., AND A. HAGEDOORN, M.D.

Amsterdam, Holland

It seems worth while to present the following case of (para) central scotoma as an initial sign of peripheral melanoblastoma of the choroid because (1) unnecessary risk for the patient and a great deal of worry for the ophthalmologist might have been avoided if a correct diagnosis had been made earlier; (2) the recent paper of Fry and McDonald[1] shows that, since the condition is rare and not yet very well understood, the same mistake is likely to be made again.

CASE HISTORY

Mr. J., aged 30 years, was seen on January 1, 1954, because of complaints suggesting asthenopia. His eyes seemed to be completely normal. Vision, O.U., was 10/10.

On February 15th he returned because, about a week before, his right eye had become blurred. Vision had decreased to 0.2; it was noted that the disc was somewhat hyperemic and the macular region slightly edematous. There was a central scotoma for colors. In the Amsler test the lines were not quite regular in a small area directly over the center. The blindspot appeared enlarged. A diagnosis of central serous retinopathy was made, although the possibility of retrobulbar neuritis was not entirely overlooked. An extensive general examination revealed no abnormalities.

In 1952, the patient had had a benign tuberculous infection of the lungs but in the present examination only small calcifications were found and no signs of activity. The neurologic examination also revealed no abnormalities.

Rest and vitamin-B complex were prescribed and his vision improved. On March 2, 1954, it was almost normal (0.9). But by March 21st it had dropped again, to 0.25 without definite edema in the macular region.

There was a small absolute scotoma over the center and an enlarged blindspot. The neurologist suggested disseminated sclerosis and salicylates and vitamin B were administered.

On April 1st a rather limited round detachment was seen in the temporal inferior region, with a few hemorrhages and pigment dots. Transillumination revealed no shadow. The detachment increased rapidly in extent. The Amsler lines were again seen normally; vision presented some difficulties in fixation, approaching 10/10.

Consultation with an experienced ophthalmologist led to a diagnosis of choroiditis exudativa tuberculo-allergica. This seemed to accord well with the relatively recent infection of the lungs. The patient was admitted to the hospital and PAS and streptomycin were administered.

On May 14th the detachment was nearly total and only a dubious amount of light perception remained. A puncture of the retroretinal space was made and the yellowish fluid was sent to Prof. Wolf's bacteriologic laboratory. No micro-organisms were found (later the cavia test was negative). A number of cells were found in the fluid but they could not be identified with any certainty. They often resembled desquamated pigmented epithelium and did not justify a diagnosis of tumor (fig. 1).

On June 24th there was a voluminous vitreous hemorrhage. X-ray treatment was given. On August 2nd acute glaucoma developed and the eye was finally enucleated. A malignant melanoma of the spindle cell type was found (fig. 2).

COMMENT

Christensen and Rowen[2] said that in some cases the cells found in the retroretinal fluid might make a diagnosis of melanoblastoma possible. In considering the pathology and the tiny walls of the blood vessels in some of these tumors we now feel that the trauma that would result from puncturing the globe in case of malignancy is not justifiable. The

* From the Eye Clinic, University of Amsterdam.

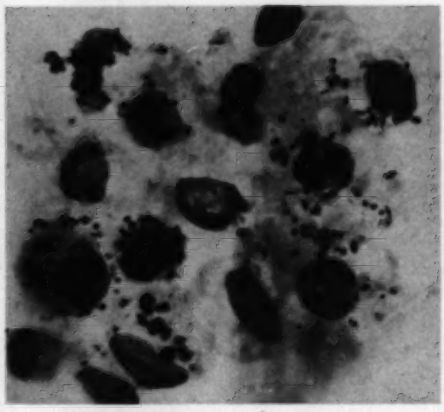

Fig. 1 (van Alphen and Hagedoorn). Cells in punctate fluid.

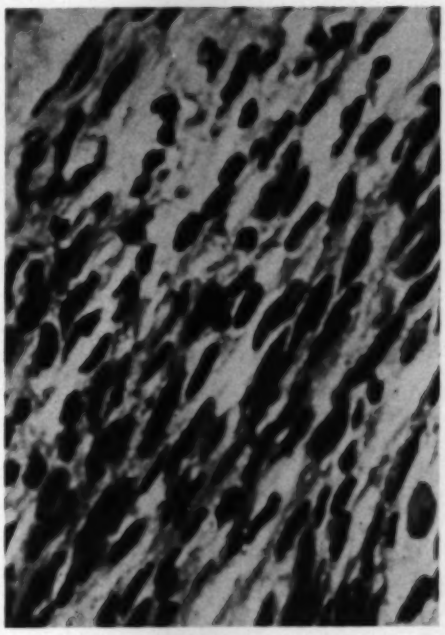

Fig. 2 (van Alphen and Hagedoorn). Aspect of tumor.

insignificant difference in life expectancy in small and more advanced tumors (Westerveld-Brandon and Zeeman[3]) even suggests that the trauma from enucleation, unless performed with extreme care, might even tend to promote metastasis. Moreover, in view of the varying aspects of the frequently detached cells of the pigmented epithelium and the rarity of tumor cells in the subretinal fluid, diagnosis may often be extremely difficult, if not impossible.

Fry and McDonald suggested the following explanation for the macular affection:

1. An extension of the area of serous edema surrounding the tumor. However, the characteristics of the detachment in the macular area in their two cases differed from those of the detachment surrounding the tumor.

2. A toxic effect on the retina at the macular area. The macular area is vulnerable!

Klien[4] confirmed the absence of reports in the literature and presented another case with intermittent disturbance of central vision. She suggested a third theory:

3. Damage to the walls of the perimacular vessels.

In a recent paper Hagedoorn[5] showed that the occurrence of minimal detachments (fig. 3) (Samuels[6]) in melanoblastoma together with the desquamation of pigment epithelial cells in the region of the tumor explains the "taches noirâtres" of Zeeman.

In Figure 3 (Case 1) of Fry and McDonald these pigmentary deposits are present in abundance. This picture supports the view that the extension of the "minimal detachment" into the macular area may explain

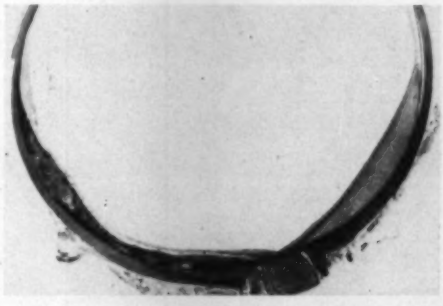

Fig. 3 (van Alphen and Hagedoorn). "Minimal detachment" in melanoblastoma (Samuels). (Figure 10 from Hagedoorn and Salim: Am. J. Ophth., 45:51-59, 1958.)

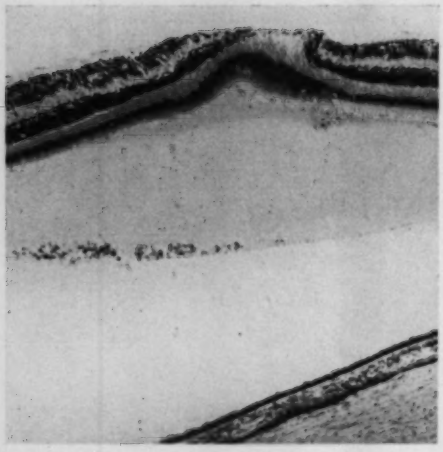

Fig. 4 (van Alphen and Hagedoorn). Macular area in melanoblastoma of the cornea. (From top to bottom) Retina, subretinal albuminous fluid, transported detached pigment epithelial cells, artificial empty space due to shrinking of the tissues in fixation, choroid and intact pigment epithelium, and sclera. (From Hagedoorn and Salim: Am. J. Ophth., 45:51-59, 1958.)

the condition. The production of this toxic fluid from the region of the tumor may reach the macular area with decrease of vision which will improve again if the fluid is resorbed. Desquamated pigment epithelial cells may be left where they are, like the debris after a flood (fig. 4).

Zeeman[7] demonstrated the vulnerability of the macula in iridocyclitis. This feature probably explains the early appearance of the central scotoma. The subretinal fluid may act either directly on the cells (Fry and McDonald) or through the intermediacy of the perimacular vessels (Klien).

Summary

A fourth case of malignant melanoma with macular symptoms as an initial clinical finding is reported. It is suggested that the involvement of the macular region is due to the extension of a minimal detachment (Samuels) to this area, which is more vulnerable than other areas of the retina. Temporary improvements in visual acuity may be explained by local resorption of the fluid.

University Eye Hospital.

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CHOROIDAL DETACHMENT FOLLOWING CATARACT EXTRACTION

A CASE REPORT

H. WALTER FORSTER, JR., M.D.
Philadelphia, Pennsylvania

L.D., a 79-year-old man, known to be diabetic since September, 1957, was first seen by me in November, 1957. At that time the best obtainable visual acuity was 6/22 in each eye. Ocular tension was 6.0 with a 5.5 gm. weight, O.U. He had cupuliform cataracts in both eyes, but, except for one small exudate below the fovea of the right eye, the fundi seemed normal for his age. Refraction showed a myopic error in both eyes and suitable glasses were prescribed.

He returned on August 8, 1958, with visual acuity of 6/22 in the right eye and 3/60 in the left, uncorrectible, and admission to Episcopal Hospital for extraction of the cataract from the left eye was arranged. On September 10th he had an uncomplicated intracapsular cataract extraction with complete iridectomy. Two 6-0 corneoscleral sutures were used and the anterior chamber was filled with air at the end of the operation.

During his hospital stay he had no difficulties, except for an allergy to Scotch tape. Surprisingly, his skin was then found to tolerate adhesive tape. At no time did he have a flat or shallow chamber or any intraocular hemorrhages. His urine was sugar free at all times on 26 units of NPH insulin and a suitable diabetic diet. He was discharged on

the eighth postoperative day, with his corneoscleral sutures in place, on one-percent atropine drops once daily and 0.5-percent prednisolone drops three times daily, with instructions as to the usual postoperative precautions.

On September 26th, the 15th postoperative day, he came to my office, at which time he was found to have moderate-sized choroidal detachments nasally and temporally, not present at the time of discharge from the hospital. The cornea had a moderate amount of edema with folds in Descemet's membrane. There was vitreous in the anterior chamber, practically in contact with the cornea at one point but the chamber was quite deep. I removed the corneoscleral sutures, stopped the atropine and started 0.25-percent Floropryl ointment nightly and continued the prednisolone drops as before. At this time the primary concern was with the corneal endothelium rather than the choroidal detachment.

Four days later the pupil was smaller. Vitreous was still present in the anterior chamber, not quite in contact with the cornea. The corneal edema, however, had cleared up considerably. The chamber was deep. There was no evidence of an iris prolapse or a wound leak but the choroidal detachments nasally and temporally were more extensive. The posterior pole of the fundus could be seen as though at the end of a tunnel. Floropryl ointment was stopped and one-percent Cyclogyl drops three times daily substituted. The prednisolone drops were continued.

Two days later, on the 21st postoperative day, he could not see at all with his left eye. On examination the left eye had no light perception. The cornea was clear. The anterior chamber was moderately deep but filled with vitreous. I was unable to see any red reflex at all with the ophthalmoscope, the choroidal detachments having come in contact with each other, obliterating the previously present tunnel to the posterior pole.

He was immediately readmitted to the hospital where he had a trephination of the sclera in the lower nasal and lower temporal quadrants. A large amount of subscleral fluid was obtained through these openings, and air injected into the anterior chamber forced the vitreous back easily. The following day light perception had returned. He was discharged on the fourth postoperative day on one-percent Cyclogyl and 0.5-percent prednisolone drops, each three times daily.

Nine days after the second operation he reported to my office with edema of the cornea, a deep anterior chamber and a tension of 2.0 with a 7.5 gm. weight in his left eye. I could see a red reflex and the choroidal detachments had disappeared. The Cyclogyl was stopped and a mixture of two-percent pilocarpine and 0.25-percent eserine (Miocel) was started four times daily. Prednisolone drops were continued. Two days later the corneal edema had cleared up, but he had an epithelial keratitis, which I attributed to the Miocel. Ocular tension was 9.0 with a 5.5 gm. weight. Miocel was discontinued and 0.75-percent Carcholin drops three times daily were substituted. Prednisolone drops were continued.

One week later, on October 22nd, he had practically no epithelial keratitis, tension was 6.0 with a 7.5 gm. weight, and there was quite a clear view of the fundus. There was some diabetic retinopathy in the macular area but with an aphakic correction 6/22 visual acuity could be obtained.

Since then on four occasions his tension has been in the middle range of normal on 0.75-percent Carcholin drops three times daily. The only exception was once when it was up to 4.0 with a 7.5 gm. weight because he had had no drops since the previous night. Gonioscopy showed an angle closed nasally and temporally on either side of the iridectomy but open below. His corrected visual acuity is now 6/12+ and he reads six-point type with a bifocal lens.

Comment

In view of the gonioscopic findings and the absence of preoperative glaucoma I suspect that the glaucoma is secondary to anterior synechias blocking the angle. Two operations must have caused enough iridocyclitis to produce this, even though there never was a flat chamber, unless the anterior chamber emptied and refilled during the week at home between his hospital discharge and first postoperative office visit.

A number of unanswered questions are posed by the development of such a massive choroidal detachment:

1. There is no unanimity of opinion regarding the need for a wound leak as a precursor to a choroidal detachment, particularly a delayed one. There was no evidence of a wound leak in this case.

2. The possibility of an allergic reaction in the choroid must be considered.

3. Does the retina overlying a choroidal detachment lose its function temporarily? Visual fields are not ordinarily done on postoperative choroidal detachments. The cornea is not usually clear enough at this stage to make careful field studies possible.

4. What happened to the vitreous at the time the patient had no light perception? The anterior chamber was full of vitreous but this could account for only a small portion of the total volume of the vitreous. There must have been a pocket of vitreous behind the contact area where the nasal and temporal choroidal detachments ballooned out and touched each other anteriorly.

There must be some decrease in the total volume of the vitreous in the presence of massive choroidal detachment for the volume of the globe remains the same.

Summary

1. A case of delayed "total" choroidal detachment following uncomplicated intracapsular cataract extraction in a 79-year-old diabetic is presented.

2. This detachment was characterized by total absence of light perception at the maximum stage of development.

3. Trephination of the sclera removed subscleral fluid and relieved the choroidal detachment, with a good functional visual result.

4. Speculation as to the fate of the vitreous during the phase of massive detachment of the choroid was considered.

37 South 20th Street (3).

LAURENCE-MOON-BIEDL SYNDROME*

M. S. Nirankari, F.R.C.S. (Edin),
S. S. Manchanda, M.D.
and
M. C. Maudgal, D.O.M.S.
Amritsar (Punjab), India

The clinical combination of retinitis pigmentosa, polydactyly, obesity, mental retardation, and hypogenitalism forms the complete picture of Laurence-Moon-Biedl syndrome. It occurs quite rarely. Approximately 284 cases have been reported so far. Only in a fraction of the reported cases has the complete syndrome been described. The following four cases of this syndrome (two each in the two families) are considered worth reporting. Except for an indefinite hypogenitalism, an almost typical entire syndrome was seen in all four cases. There was no evidence of a hereditary influence.

Case reports

Case 1

A 14-year-old Hindu girl (fig. 1) was admitted on January 1, 1958. She complained of poor vision, particularly in darkness for about 10 years. She was a rather heavy child, steadily getting more and more obese despite a restricted diet. She was very poor at school and as she could not progress beyond the third primary standard, she was taken out of school.

She was the third in a family of 11 children of unrelated parents and was a full-term child. There was nothing relevant in the past history. Development was slow. She began sitting and standing without support at 12 and 20 months, respectively, and had a monosyllabic speech without meaning at two years. She started menses six months ago; the flow was scanty and irregular. Excepting her younger brother (Case 2) who was similarly affected, there was no family history of obesity, visual disturbance or polysyndactyly. Four sisters and one brother were normal. There were two deaths from acute febrile illness and two abortions.

On physical examination, the patient was obese, with selective fat deposition on the hips, abdomen, and breast. Her weight was 115 lb., height 59 inches, head circumference 20.8 inches, chest 33 inches and abdomen (at umbilicus, lying and fasting) 33.5 inches. A supernumerary digit was present on both the feet and the right hand (total 23). She

Fig. 1 (Nirankari and Manchanda). This 14-year-old patient shows polydactyly and obesity.

* From the Medical College of Amritsar.

was mentally backward, could not count to one hundred nor do simple addition and subtraction. She presented a dull look with a placid and vacant expression.

The fundus was myopic and tigroid in appearance. The disc appeared normal. The arteries were narrow and, at the periphery of the fundus, there were narrow streaks of black pigment along the blood vessels. The pigment deposits did not resemble bone corpuscles. Choroidal degeneration was present. There was myopia of —5.5D. in the right eye and —7.5D. in the left eye, not improved with glasses.

Routine laboratory investigations, total and differential counts, blood sugar curve, serum cholesterol, blood urea, serology for syphilis, R.H. grouping, complete urine examination, including specific gravity test and electrocardiographic tracing, and so forth, were completely unhelpful. Skiagram of the skull did not reveal anything abnormal. The hypophyseal fossa was of normal size and shape.

CASE 2

V., aged four and one-half years (figs. 2 and 3) was the younger brother of the patient in Case 1. This child was also mentally backward, with a history of delayed head lifting, sitting, standing, walking, and talking. The child has been steadily becoming obese for about the past one and one-half years. He also could not see in the dark. His weight was 39 lb., height 40.5 inches, head circumference 19.9 inches, chest 22.2 inches, and abdomen 23.4 inches. An extra phalanx was present on both hands and both feet.

The fundus had a tigroid appearance and showed degeneration of the choriocapillaris. No pigmentation or attenuation of the blood vessels was present. Only choroidal degeneration was present. The refraction was myopic, —10.0D., right eye, and —8.0D., left eye. The vision did not improve with glasses. Both testicles could be palpated in the scrotum. No abnormality was found in any other system of the body. The laboratory tests as in Case 1 were negative.

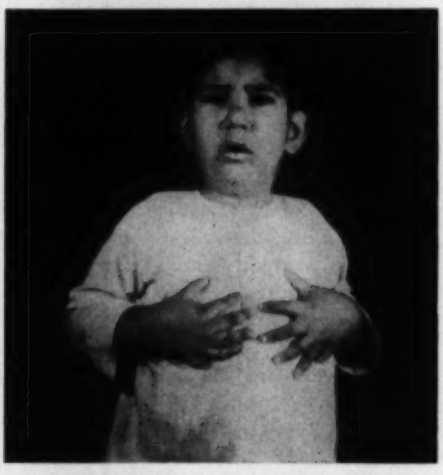

Fig. 2 (Nirankari and Manchanda). Case 2. Patient aged four and one-half years, shows obesity, vacant look and polydactyly.

Fig. 3 (Nirankari and Manchanda). Same patient as in Figure 2, showing polydactyly and normal genitalia.

CASE 3

G., aged 10 years, a boy (fig. 4) was admitted on June 10, 1958. He belonged to the second family, herein reported, which was unrelated to the first family. The patient was presented for cough with expectoration of about two months' duration. On interrogation the patient was stated to be abnormally obese from childhood and suffered from defective vision (more marked in the darkness) and mental backwardness. The child was the fifth birth, born at full-term and was rather heavy at birth. He had extra phalanges in each limb, the extra phalanx was a rudimentary one and the father tied a thread tightly around it, and in time the extra phalanx withered off.

Various milestones of development were delayed and, at the age of six years when sent to school, he made hardly any progress, being unable even to learn the alphabet. Defective vision, more pronounced at night, was first noticed at the age of three years and has progressed since then. There was nothing significant in the past or family histories; nor was there a history of consanguinity. The

younger brother (Case 4) was likewise affected. There had been a total of seven pregnancies; three children had died during infancy and childhood from gastroenteritis and some febrile illnesses.

Physical examination revealed an obese child with more deposits of fat on the chest and obdomen. The facies were full, and moonlike and the expression rather vacant. There was polysyndactyly of six toes on each foot and five fingers on each hand, with a small stump at the base of the right little finger. The vision was much reduced and there was generalized peripheral contraction of the field of vision. Bilateral early optic atrophy and choroidal degeneration were seen. There were slight changes resembling retinitis pigmentosa. The child was mentally backward and could count only up to 10. He could memorize nothing. He could, however, recognize common objects and dress and undress himself.

In the lungs, there were signs of consolidation over the right upper zone. Other systems were normal. The various laboratory investigations were normal. X-ray films of the chest confirmed consolidation in the right subapical region. The skiagram of the skull was normal.

CASE 4

J., a six-year-old boy (fig. 4) the younger brother of the patient in Case 3 was born normally at full-term. He had, however, six phalanges on each limb. By the end of the first year, he started getting more and more fat and by the age of two years, the mother noticed that the child could not see properly in the dark. The child was also mentally backward. His weight was 54 lb. and he had six toes on each foot and six fingers on the left hand.

Fundus examination revealed chorioretinal degeneration with marked attenuation of the blood vessels, the disc was pale. Pigmentary disturbance was not seen. No abnormality was detected in any other system.

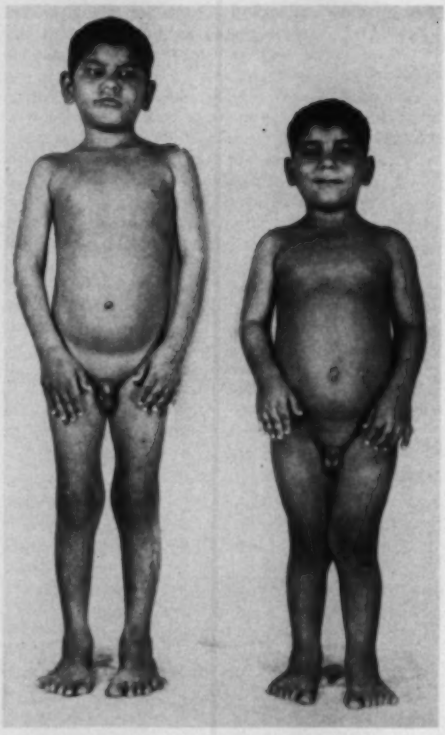

Fig. 4 (Nirankari and Manchanda). Cases 3 and 4, two brothers, showing obesity, polydactyly and normal genitalia.

COMMENTS

The manifestations of the syndrome known as Laurence-Moon-Biedl syndrome include the presence of nyctalopia, obesity, mental retardation, polydactyly and hypogenitalism. The association of these features was first pointed out by Laurence and Moon (1866). They noted the existence of such unusual features as mental deficiency, hypogenitalism, and obesity in four cases of retinitis pigmentosa.

Bardet (1920) mentioned the presence of polydactyly as an additional feature and in 1923 Bardet pointed out the familial incidence of the syndrome. A number of other anomalies have been reported in cases of this syndrome, for instance, deafness, microphthalmia, squint, nystagmus, myopia, ptosis, congenital heart diseases, hypospadias, tetany, dwarfism, and bilateral genu valgum, and so forth. The basic anomaly is a dystrophy in eyes, genitals, skeleton, nervous system, and deranged fat metabolism.

François and Bello (1952) pointed out the existence of great variations in the ocular manifestations of the syndrome. Fundus changes of a type resembling retinitis pigmentosa frequently occur in this disease. Abnormal pigmentation may be slight or absent. Ellis and Law (1941) and Taylor (1947) have pointed out fundus changes may be of four types: (1) typical retinitis pigmentosa; (2) atypical retinitis pigmentosa, with increased pigmentary disturbance in the central area of the fundus rather than the periphery; (3) macular dystrophy; (4)

atypical retinitis pigmentosa combined with macular dystrophy.

In the cases reported here, the fundus picture resembled retinitis pigmentosa of an atypical type. The pigmentary changes were not at all characteristic of retinitis pigmentosa. In Case 2, there was only choroidal degeneration but there was a typical history of nyctalopia. In our experience the fundus changes are not necessarily those of retinitis pigmentosa but rather a chorioretinal degeneration. Evidence of this may be attenuation of the blood vessels, degeneration of the choriocapillaris and pigmentary changes, which may be typical bone corpuscle in type or streaks of pigment deposits along the blood vessels. In the earlier stages and in young patients as in our Cases 2 and 4, there may not be any visible pigmentary change on funduscopy. The different features of tapetoretinal degeneration appear later on when the disease is fairly far advanced. A typical history of nyctalopia is enough to warrant a diagnosis of Laurence-Moon-Biedl syndrome provided other features of the syndrome are present. In all our four cases, mental backwardness, obesity, and polydactyly were present. Definite evidence of hypogenitalism was the only lacking feature in these cases.

Transmission of the disease is said to be principally by recessive heredity and through polygenetic genes. In the cases reported, however, there is no hereditary evidence. It is possible the disease may be a mutation, just cropping up occasionally.

Summary

Four typical cases of Laurence-Moon-Biedl syndrome are described. These cases were in two unrelated families—a brother and sister in one and two brothers in the other.

There was no history of consanguinity of parents in either family.

Department of Ophthalmology.

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AMYLOID DISEASE OF CONJUNCTIVA AND TARSUS*

A CASE REPORT

DUPONT GUERRY, III, M.D.

AND

HERBERT WIESINGER, M.D.

Richmond, Virginia

Amyloid disease of the conjunctiva and lid is a rare but well-authenticated entity. Although it was investigated in Russia before the turn of the century (Raehrman, Kubli, and Vossius), reports in the English literature are few in number. Redi and Chinaglia reported localized amyloid degeneration of the conjunctiva in cases of chronic trachoma, while Wahi and Wahi describe a case in India without suggesting an etiologic agent. Ellis in her report suggested nutritional deficiency as a possible etiologic factor and Ashton described amyloid degeneration as a subgroup of the hyalin infiltrations of the eyelids. In this respect he followed Duke-Elder and Schmiedeberg, who

* From the Department of Ophthalmology, Medical College of Virginia.

Fig. 1 (Guerry and Wiesinger). Amyloidosis of right upper lid.

consider hyalin as a transitional product in the formation of amyloid albumin from albumin. All authors are in general agreement on the histologic findings and the obscure etiology. Although cases have been reported in association with such chronic inflammatory conditions as trachoma, most cases are found in otherwise healthy eyes of normal individuals.

Case report

In this paper we wish to report a case of primary amyloidosis of the eyelids and conjunctiva of unknown etiology, occurring in a 62-year-old white married woman.

This patient was referred to us in May, 1957, with the complaint of "inflamed left eye all the previous winter," thought to be of allergic origin. Various salves had been prescribed without relief and conjunctival cauterization had been carried out in the lower cul-de-sac without improvement.

Fig. 2 (Guerry and Wiesinger), Appearance of left upper lid before operation.

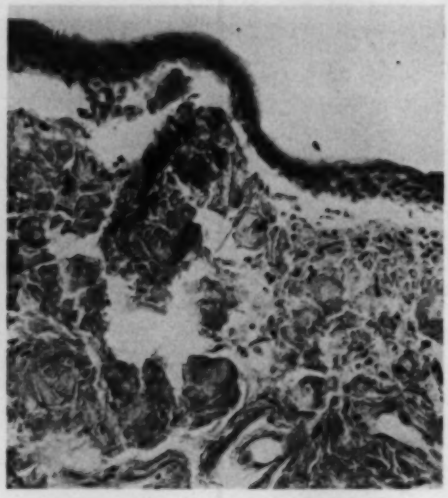

Fig. 3 (Guerry and Wiesinger). Histologic section of excised tarsal plate.

On examination the right eye was found to be normal. The entire left lower cul-de-sac was involved in a fairly dense mass of grayish-white tissue where cauterization had been carried out. The lower border of the tarsus seemed to be involved in this process and, in addition, appeared infiltrated with a brownish-yellow amorphous material. The outer region of the upper tarsal conjunctiva revealed a similar picture. Localized amyloidosis was suspected and confirmed by biopsy of the lower tarsus through a small skin incision. The patient was subjectively improved after removal of this tissue.

She was seen again in January, 1958, with the complaint of a similar process beginning in the right eye. The right upper lid showed incomplete ptosis; the lid was markedly thickened and upon eversion it was seen that the greater part of the tarsal plate was heavily infiltrated by friable brownish-yellow material distributed in a nodular fashion and with echymotic spots scattered throughout. The previously seen mass in the left lower cul-de-sac was greatly increased in size and was very friable when picked up with forceps.

By November, 1958, ptosis of the right upper lid had become bothersome to the patient. The heavy, thickened lid could barely be lifted above the pupil and this with great difficulty (fig. 1). The entire upper tarsal plate and tarsal conjunctiva had been replaced by amorphous brownish material which biopsy proved to be amyloid tissue. The left lower cul-de-sac had become even more infiltrated than before and by now two thirds of the left upper lid (fig. 2) was involved.

On November 18, 1958, the right upper tarsal plate (with the exception of a one-to-two-mm. border at the lid margin) along with the involved conjunctiva was excised. The remaining tarsal strip was sutured to the conjunctiva and levator edge.

This procedure had an excellent cosmetic and functional result. The ptosis disappeared entirely, the lid was reduced to almost normal thickness and function was fully restored. Although the other lids have not yet reached the point where surgical intervention is necessary it will not be long before surgery will be indicated.

Thorough general studies revealed the patient to be in good health. The only abnormality noted was a hypercholesteremia of 471 and a cholelithiasis which necessitated a cholecystectomy. Liver biopsy taken at surgery was essentially normal.

Histology

Histologic section of the excised tarsal plate (fig. 3) shows the tarsus to be replaced by a diffuse nonencapsulated mass consisting of ellipsoidal circular and irregular acellular masses of an eosinophilic staining material, occasionally separated by strands of fibrous tissue. Chronic inflammatary cells are seen in varying numbers, as well as occasional plasma cells and giant cells. Some of these homogenous masses surrounded small blood vessels, partially or totally obliterating their lumina. In selective stainings by Congo red and iodine these masses give the reaction of amyloid.

Summary

A case of localized amyloidosis involving the tarsal plates of all four eyelids and considerable bulbar and palpebral conjunctiva is reported. The eyes were otherwise normal and the patient's general physical condition was normal except for moderate hypercholesteremia and cholelithiasis. There was no evidence of general amyloidosis.

2015 Monument Avenue (20).

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PRIMITIVE LYMPHOMATOUS HYPERPLASIA*

Of the Palpebral Conjunctiva, Conjunctival Cul-de-sac and Plica Semilunaris

José Sverdlick, M.D.
Buenos Aires, Argentina

Lymphoid tissue of the eye and its adnexa is preferentially situated in the palpebral conjunctiva, conjunctival cul-de-sac, plica semilunaris, and in the orbit. The cells forming it are lymphocytes, lymphoblasts, histiocytes (reticular cells) and plasmic cells (plasmazellen) and have the same morphologic and structural characteristics as the cytologic elements constituting the lymphohematopoietic tissue.

The pathology of ocular lymphoid tissue is extremely rare, the histopathologic changes causing its development are not often found. These changes, seen in the form of diffuse or localized hyperplasia, hypertrophies or tumorlike formations, originate in the lymphatic cells composing its structure. When the cells contributing to its formation are lymphocytes, lymphoblasts, histiocytes and plasmazellen, they are differentiated, anatomopathologically, as lymphocytomas, lymphoblastomas, histiocytomas, and plasmomas, respectively.

In those cases in which are mixed several

* From the Buenos Aires Medical School.

Fig. 1. (Sverdlick). Prolific and exuberant growths in the plica semilunaris.

different morphologic types of cells, giving a polymorphous appearance to the histologic image, it is better to use the term lymphomatosis or lymphoblastomatosis, as being less ambiguous.

Ocular lymphomatosis is found in two clinical forms: (a) primitive, strictly localized in the ocular lymphoid system; (b) secondary, associated with manifestations of the lymphohematopoietic system.

The ophthalmologist is particularly interested in the primitive form because of the difficulties in diagnosis, it being easier to arrive at a diagnosis in the secondary form because of the number of signs and biologic and clinical symptoms which accompany the ophthalmologic observations.

Case report

Clinical history. A 20-year-old woman came to the consulting rooms on March 18, 1949, with bilateral palpebral edema, intense lacrimation, and photophobia, from which she had been suffering for approximately seven months.

Eye examination showed: Left eye. Moderate palpebral ptosis. Inspection showed the plica semilunaris region to be occupied by a pinkish-colored growth of a gelatinous aspect (fig. 1) with intense superficial vascularization of a cauliflowerlike appearance, and exploration proved this to come from the upper conjunctival cul-de-sac. On eversion of the upper eyelid, lesions were found which made it necessary to divide the conjunctival surface into three zones for study (fig. 2):

Fig. 2 (Sverdlick). Except for the center area, polypoid formations are distributed through the upper palpebral conjunctiva.

a. Internal zone, which was occupied by numerous pinkish colored, rounded formations, with a polypoid aspect, superficially vascularized and divided by fissures and narrow grooves.

b. Middle zone. The conjunctival surface was smooth and even, with none of these excrescences, except in the vicinity of the conjunctival cul-de-sac.

c. External zone. Here the growth was well developed and extended toward the conjunctival cul-de-sac, which was completely occupied. In the lower conjunctival cul-de-sac three gigantic growths only were seen.

Right eye. The upper palpebral conjunctiva showed no neoformation, though the corresponding conjunctival cul-de-sac was completely occupied by a diffuse infiltration, a kind of swelling outward, causing a hernia toward the exterior. A deep groove divided this exuberant conjunctival mass into two lobes (fig. 3) which extended from the external canthus to the plica semilunaris, which also had a proliferated appearance.

The fundi were normal, as were the lacrimal, parotid, submaxillar, and sublingual glands. The hemogram was normal. Clinical, radiologic and biologic examinations were all normal.

Commentary

In view of the fact that the lesions were localized exclusively in the ophthamologic sphere, with no systemic participation and with a normal blood picture, ocular lymphomatosis was suspected and a biopsy, which was performed immediately, proved this diagnosis to be correct and also indicated the

treatment to be carried out. In fact, four radiotherapy sessions were sufficient to cause complete disappearance of the lesions.

From the photomicrograph (fig. 4) it can be seen how the subepithelial conjunctival tissue is totally occupied by cellular elements of a genuine lymphatic strain, such as lymphocytes, lymphoblasts, and reticular cells; the association of these gives us a true polymorphous histologic picture.

Pascheff (1930, 1932) made a detailed study of the histopathology of chronic hyperplasias of the conjunctiva, especially conjunctival lymphomatous hyperplasia, and pointed out its extreme rarity. Pascheff's anatomic-clinical classification, which is almost unknown and has been quite unjustly ignored in the majority of publications and papers published on ocular lymphomatosis since 1930 is:

1. Plasmocellular hyperplasia: (a) diffuse: plasmocellular conjunctivitis, (b) localized plasmoma.

2. Lymphomatous hyperplasia: (a) aleukemic conjunctival hyperplasia (diffuse or localized), (b) leukemic conjunctival hyperplasia, (c) associated with cutaneous hyperplasia, (d) of orbital origin (Mickulicz' syndrome).

3. Follicular hyperplasia: (a) simple follicular hyperplasia (follicular conjunctivitis), (b) miliary follicular hyperplasia, (c) confluent follicular hyperplasia.

Fig. 3 (Sverdlick). Conjunctival cul-de-sac, showing the extent of the diffuse infiltration and an outward swelling, causing a bilobulated hernia toward the exterior.

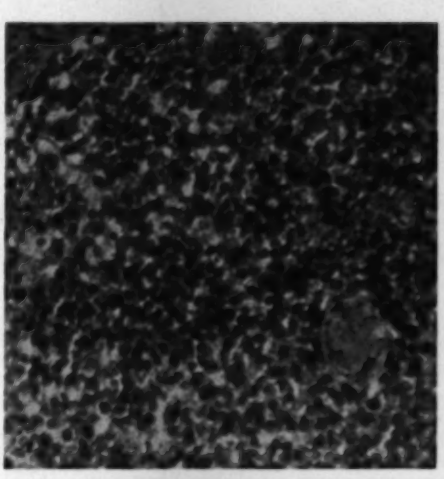

Fig. 4 (Sverdlick). The subepithelial conjunctival tissue is totally occupied by genuine lymphatic cellular elements, such as lymphoblasts, lymphocytes and reticular cells which are intermixed, giving a true polymorphous histologic picture.

4. Papillary hyperplasia: (a) simple papillary hyperplasia (catarrhal conjunctivitis), (b) follicular lymphopapillary hyperplasia, (c) fibropapillary hyperplasia (vernal conjunctivitis).

5. Hyaloid hyperplasia: (a) primitive, (b) secondary.

Primitive ocular lymphomatous hyperplasia is a disease sensitive to roentgen therapy and, when localized in the conjunctiva, it can easily be confused with vernal conjunctivitis, follicular conjunctivitis, trachoma, Parinaud's conjunctivitis, conjunctival tuberculosis, and Mickulicz' syndrome. The best way to get the correct diagnosis is by biopsy, which should be performed immediately an atypical polymorphous conjunctival picture is found.

Summary

Disease of the lymphatic tissue of the globe and its adnexa is very rarely seen. The case reported shows ocular lesions characterized by polypoid formations distributed in

the upper palpebral conjunctiva, prolific growths in the plica semilunaris, and exuberant, diffuse infiltration of the lower conjunctival cul-de-sac, with a complete absence of changes in the lymphohematopoietic system (primitive ocular lymphomatosis).

Polymorphism of the ocular lesions caused me to suspect lymphomatosis and a biopsy proved the diagnosis to be correct. Four sessions of radiotherapy were sufficient to produce complete disappearance of the lesions.

Bmé. Mitre 1427.

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FREQUENCY OF MYOPIA GRAVIS

Adalbert Fuchs, M.D.

Meran, Italy

Questionnaires were sent to 1,028 eye hospitals or departments; 367 (35.6 percent) were returned, most of them properly completed. The information I culled from the questionnaires for high myopia (more than −7.0D.) is quite uncertain. In 116 questionnaires the space for it was either empty or there was a zero or a question mark. Apparently the figure for high myopia in some cases represented all myopia.

I had always thought that high myopia is especially frequent among Jews, Arabs, Parsees, and Japanese. The questionnaires did not confirm this opinion. In Japan, however, where the questionnaires were very carefully completed, seven of 31 hospitals reported an especially high incidence of myopia gravis. Jutendo College in Tokyo noted that 100 cases had been operated for myopia, which shows a high frequency of myopia gravis. The results of the survey are given in Table 1. No percentages are given in the table because it was uncertain whether the figures really referred to high myopia (over −7.0D.). This table shows an especially high incidence of myopia gravis in the cities of Spain and Italy.

Since in my experience a number of cases of progressive myopia in early childhood

TABLE 1

RELATION BETWEEN CATARACT EXTRACTIONS AND NEW PATIENTS AND MYOPIA GRAVIS

Location of Hospital	Cataract Extractions	New Patients in One Year	Myopia Gravis
Santiago, Chile	193	6,727	150
Lille, France	102	4,018	129
Marburg, Germany	121	5,400	151
Berlin, Germany	145	4,320	120
Rostock, Germany	181	18,744	245
Jena, Germany	133	21,000	206
Berlin, Germany	373	22,014	440
Nordhausen, Germany	49	10,791	156
Geneva, Switzerland	108	5,201	127
Vienna I, Austria	317	15,176	318
Vienna II, Austria	550	17,000	284
Sarajevo, Jugoslavia	276	7,680	132
Bratislava, Czechoslovakia	235	13,405	138
Barcelona, Spain	92	3,012	122
Barcelona, Spain	40	3,000	400
Pamplona, Spain	97	800	305
Sevilla, Spain	25	3,485	158
Rome, Italy	326	17,380	318
Bologna, Italy	324	18,506	225
Milano, Italy	182	17,500	1,000
Milano, Italy	194	23,550	515
Pisa, Italy	170	4,900	400
Naples, Italy	168	11,114	100
Florence, Italy	49	7,461	197
Cagliari, Italy	231	4,000	200
Budapest, Hungary	407	16,698	324
Georgic, SSR	442	12,818	531
Rangoon, Burma	278	12,066	260
Hokkaido, Japan	14	2,979	111
Amori-ken, Japan	35	2,500	100
Kanazawa, Japan	29	3,366	177
Niigate, Japan	56	4,523	177
Tokyo, Juntendo, Japan	92	6,272	1,500
Kyoto, Japan	56	5,607	252
Fukuoka, Japan	57	5,354	244
Taipeh, Taiwan, Nat. Defense Center	4	5,250	128
Alexandria, Egypt	555	41,260	341
Cairo, Egypt	62	135,510	120

could be halted by local and general treatment, I believe that heredity as a cause is quite overestimated by many eye doctors and that a certain softness of the sclera is due to inadequate nutrition.[1]

Nowak[2] was amazed that, in Iowa, in spite of the large number of patients he had to examine, he sometimes did not see a myopic person for a whole week, while in Vienna he saw at least one myopia case a day among his patients. Nowak quoted others that myopia is more frequent in such big cities as Chicago and New York. Nowak found that the majority of myopic patients were immigrants and he was of the opinion that the frequency of myopia among them was nearly the same as in the European countries from which these patients had come. A great difference was found in the group of the first generation, born in the United States where the number of myopic persons is much smaller. The children of the immigrants showed not only less "school-myopia" but also less progressive myopia than their parents. Since Nowak had the opportunity to observe hundreds of children during their school terms, his findings are especially significant.

Of interest in Nowak's report are the married couples who were both myopic for, according to Steiger, myopia is hereditary. In 16 years Nowak found only three married couples both myopic. Of these, the first couple had no children and the second, three very small children too young for his research. The third married couple, however, were immigrants from Luxembourg to Iowa and nearly the same age. The husband had −3.0D., his wife −14.0D., and −15.0D. Their nine children—the youngest was 14 years of age when Nowak examined him—were all hypermetropic; not a single one was myopic.

The findings of Nowak are similar to mine at the New York Eye and Ear Infirmary (1947-1955). I was amazed at the low incidence of high myopia, as well as of large circumpapillary atrophy of the choroid. Nowak's study is most interesting because it shows a considerable influence of the soil or nutrition upon the state of refraction. It would be worth while to compile and compare statistics of myopia in different countries. This would not be difficult since refraction statistics for school children would be available in many countries.

Karl Wolfstrasse 14.

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TUMOR OF THE LACRIMAL SAC*

O. A. Brown, M.D.
Taxila, West Pakistan

Tumors of the lacrimal sac are uncommon. For this reason the following case is presented.

Case report

Y. S. (No. 1279-59), a 45-year-old Pakistani man, was admitted because of swelling in the area of the right lacrimal sac. This swelling had been present for one year. The patient gave no history of previous lacrimation or symptoms of dacrocystitis.

Examination showed obvious swelling over the lacrimal sac of the right eye. This swelling was firm and did not reduce with pressure. There was no reflux of pus or mucus. There was scarring of the cornea, probably due to previous infection which went untreated.

At operation a moderately large tumor was removed from the region of the lacrimal sac of the right eye. This tumor had extended up to the mucosa of the lower lid. The sac itself was not recognizable as a separate structure. The specimen was sent to the Armed Forces Institute of Pathology, Washington, D.C., where microscopic diagnosis was made: (AFIP918104): Lacrimal sac: squamous-cell carcinoma.

Comment

The immediate postoperative course was uneventful and uncomplicated. Because of the poor economic status of the patient, radiation therapy was not available. There has been no follow-up of this case. However, this is not an unusual situation, as Ellis (Am. J. Ophth., **44**: 759 [Dec.] 1957) explains, many problems of ophthalmic surgery in this subcontinent, due to the economic status of the people and other factors, are often beyond the control of the ophthalmic surgeon.

The Christian Hospital.

* From the Christian Hospital.

MULTIPLE-PURPOSE UTILITY INSTRUMENT*

Leland F. Carter, M.D.
Detroit, Michigan

This instrument has been found to have the usefulness of three instruments conveniently combined in one.

The forked end is semicurved and sharp pointed. It serves well as a scleral pick where transfixation of the globe is desired.

Fig. 1 (Carter). Multiple-purpose instrument.

The reverse side of the forked end, when used as counter pressure, is quite helpful in threading recalcitrant needles through resistant tissues. This is particularly true in muscle and scleral surgery.

On the opposite end of the instrument is a half-curved fine, yet blunt, hook readily accessible for retrieving preplaced sutures and in the arrangement of the loops. As was intended by its original designer, it also continues to be serviceable as an iris hook.

613-617 David Whitney Building (26).

* Made by the Storz Surgical Instruments of Saint Louis, Missouri.

OPHTHALMIC RESEARCH

EDITED BY FRANK W. NEWELL, M.D.
950 East 59th Street, Chicago 37, Illinois

Abstracts of papers presented at the meeting of the Eastern Section of the Association for Research in Ophthalmology, Inc., at the Wills Eye Hospital, Philadelphia, Pennsylvania, February 18, 1960.
Thomas R. Hedges, Jr., M.D., *Section Secretary*

The fine structure of the human cornea. Marie A. Jakus, Ph.D., Retina Foundation, Massachusetts Eye and Ear Infirmary, and Harvard University, Boston.

The fine structure of the human cornea, as seen in thin sections with the electron microscope, will be described. Particular emphasis will be placed upon those structures which are poorly, or not at all, resolved by the light microscope: the desmosomes between epithelial cells and between the epithelium and the basement membrane; the structure of Bowman's layer of the stroma; the stroma cells and their relationship to the stroma collagen; the organization of Descemet's membrane; and details of the endothelial cells.

Endocrine factors and the development of corneal transparency. Alfred J. Coulombre, Ph.D. and Jane L. Coulombre, B.S., Department of Anatomy, Yale University School of Medicine, New Haven, Connecticut.

The cornea of the embryonic chick has been shown to become progressively more opaque until, at about 14 days of incubation, it transmits about 40 percent of incident light. Between the 14th and 19th days of incubation the cornea rapidly becomes transparent, achieving the adult level of 96 percent transmission. This change is accompanied by a progressive, relative dehydration of the cornea, and by a deposition of metachromatic mucopolysaccharide in the stroma.

When the pituitaries of hatching chicks are grafted to the chorioallantoic membranes of seven-day host embryos the cornea becomes transparent, dehydrates and the stroma becomes metachromatic, prematurely. When l-thyroxin is administered to chick embryos between the seventh and 12th days of incubation similar results are obtained. Thiouracil, administered between the seventh and 12th days results in a retardation of corneal clearing, dehydration and the spread of metachromasia. Thus endocrine manipulation can advance or retard the development of corneal transparency but does not uncouple the three endpoints studied.

Further investigation of the organ specificity of the lens. W. Manski, Ph.D., T. Auerbach, M.A., and S. P. Halbert, M.D., Department of Ophthalmology, College of Physicians and Surgeons, Columbia University, New York.

The extensive immunologic cross reactivity of ocular lens among divergent animal species has long been known and has been termed organ specificity. Until recently, the basis of lens organ specificity could not be clearly established because of the inadequacy of the technics available. An intensive study of these phenomena are now being carried out in this laboratory utilizing the Grabar-Williams immunoelectrophoretic method. Lens antisera were prepared in the rabbit, using as antigen either human cataract or adult rabbit lens pools. These anti-sera were tested against lenses of 13 different vertebrate and two invertebrate species.

Most of the mammalian lenses reacting with antihuman cataract serum showed the presence of a minimum of nine distinct components. In several instances at least 10 cross reactions were evident. The number of cross reacting components with antihuman lens sera were fewer with chicken lens, which showed seven components. Six were found with frog lens, and five with fish. No cross reactions were detected with the squid or lobster lens. This diminishing number of components parallels the phylogenetic sequence of the various vertebrate species tested.

In the tests with homologous antirabbit lens sera, the cross reactions with mammalian lens species were also rather uniform, although the number of cross reacting components were only four in number. As with the heterologous antilens sera the number of cross reactions decreased with chicken and frog lenses (to three) and with fish lenses (to two). No reactions were seen with the invertebrate lenses. It was found that the precipitates with homologous anti-lens antibodies develop much more slowly than do the precipitates with heterologous antibodies. In addition, it appeared that the homologous anti-lens antibodies do not precipitate with the α electrophoretic family of lens antigens, in strong contrast to the multiple system found with heterologous anti-lens antibodies. This did not apply to the α crystalline group which was found to be the same in both.

The occurrence of proteases in the lens active under acidic pH. Anima Devi, Ph.D., Department of Ophthalmology, College of Physicians and Surgeons, Columbia University, New York.

The occurrence of enzymes in animal tissues

which hydrolyse proteins under acid and alkali condition has often been reported. Proteases optimally active around pH 4.0 have been identified in lung, rabbit muscle and lymphatic organ by many investigators. The importance of intracellular enzyme in autolysis and exogenous protein hydrolysis has been well recognized. The autolysis of lens protein homogenate on standing, was first reported by Krause (1935). The further studies of Zeller and Devi have provided evidences for the presence of chymotrypsin-like enzyme in bovine lens.

The present communication describes the occurrence of an enzyme which hydrolyses urea denatured hemoglobin under acid conditions. The extent of proteolysis was followed spectrophotometrically. The intracellular enzyme, present in the homogenates of bovine lens is active over a wide pH range (3.2-4.6 and 6.0-8.5, maximally active at pH 3.8 and 7.0).

This enzyme retains its activity even after prolonged dialysis against 0.005 M phosphate buffer of pH 7.2 but slowly loses its ability to digest proteins on standing at room temperatures (30°-32°C.). As a result an increase of five folds in absorption at 280mμ was noted. Autolysis can also occur at ice box temperature (2°-5°C.) but requires much longer time. The exogenous protein hydrolysis could, however, be totally prevented at deep freeze temperature (—15°C.). Th activity of this enzyme is not influenced by the divalent metallic ions like Mg, Mn, Zn, Ca.

The enzyme active at pH 3.8 has been characterized further with regard to its specificity toward synthetic substrates. The homogenate was separately incubated with (a) cbz-L-glutamyl-L-tyrosine (substrate for pepsin) at pH 3.0, 3.5, 4.0, 4.5, and 5.0; with (b) benzoyl-L-arginine methyl ester (substrate for trypsin) at pH 6.0, 7.0, 8.0, 9.0, with (c) N-acetyl-L-tyrosine ethyl ester (substrate for chymotrypsin) at pH 6.0, 7.0, 8.0, 9.0 and with (d) cbz-glycyl-L-phenylalanine (substrate for carboxypeptidase) at pH 8.0 and 9.0.

The reaction mixtures after incubation were centrifuged, and the supernatants used for chromotographic analysis. The solvents used were: (a) n-butanol :acitic acid :water (4 :1 :5) for arginine derivatives and tyrosine, (b) n-butanol : pyridine :water (4 :1 :5) for arginine and (c) n-butanol :ethanol :water (4 :1 :5) for tyrosine derivatives, (d) butanol + butanone :water :diethylamine (10 :10 :5 :1) for alanine. The detection of the hydrolyzed amino acids on the paper required Ninhydrin for tyrosine, Sakaguchi reagent for arginine, Pauly reagent for tyrosine derivative and ninhydrine for alanine respectively.

From these experiments one can conclude that bovine lens homogenate contains enzymes similar to Cathepsin A (pepsinlike), and Cathepsin C (chymotrypsinlike) and both are responsible for autolysis of exogenous proteins of the bovine lens on standing at room temperature. The purification of the enzyme active at pH 3.8 and its properties will also be discussed in the present communication.

Carbohydrate metabolism in the aging rat lens. Sidney Lerman, M.D., and Betty K. Ishida, B.A., University of Rochester School of Medicine and Dentistry, Rochester, New York.

Experiments recently completed in this laboratory indicate that the hexose monophosphate shunt is of considerable importance in the metabolic economy of the young and rapidly growing lens derived from the 26-36 day old rat. The direct oxidative pathway is apparently important during this period of lens development and the cataractogenic action of galactose may be due to the fact that it specifically inhibits glucose-6-phosphate dehydrogenase (both in vivo and in vitro) thereby resulting in a rapid and marked inhibition of the shunt.

As the animal ages, galactose becomes considerably less effective as a cataractogenic agent. In the young rat (26-32 days) one can obtain dense opacification of the lens after the animal has been maintained on a 70-percent galactose diet for 12-18 days. As the animal ages the length of time required for cataract formation increases progressively, and the 90-115 day rat can be kept on this diet for four to six weeks without developing any gross evidence of lens opacification.

Since the age of the animal is an important factor in the development of this form of experimental cataract, it might be related to the relative importance of the hexose monophosphate shunt in the lens of the young and aging rat. This pathway of glucose metabolism was therefore investigated by means of incubation experiments employing glucose-1-C^{14} and glucose-6-C^{14} as the substrates and comparing the ratio of $C^{14}O_2$ recovery from the number one and number six carbon atom in the young and aging rat lens. The enzyme G-6-P dehydrogenase was also assayed in these lenses as well as the relative rates of pyridine nucleotide transhydrogenase.

Autoradiographic localization of tritium in lens epithelium. Clifford V. Harding, Ph.D., and B. D. Srinivasan, A.B. Departments of Physiology and Ophthalmology, Columbia University, New York.

A technique has been developed for the autoradiographic localization of tritium in whole-mount preparations of lens epithelium. If the lens capsule remains between the layer of cells and the film (which is the result of the usual whole-mount procedure), most of the β-radiation from tritium localized in the cell nuclei is absorbed by the capsule before reaching the film. A modified technique enables the mounting of epithelium in such a manner that the cells are in immediate contact with the autoradiographic stripping film. This procedure has been used for detecting the incorporation of thymidine (a specific precursor to DNA synthesis) by the cells under various conditions.

In preparations of normal lens epithelium the cells which incorporate thymidine are, for the most part, restricted to the germinative zone. Cells in the central region of the epithelial layer

can, however, be induced by injury to incorporate thymidine.

Electron microscope observations on human senile cataract. Theodor Wanko, M.D., and Mary Ann Gavin, M.A., Ophthalmology Branch, National Institutes of Health, Bethesda, Maryland.

Initial studies of epithelium prepared from human cataractous lenses indicate that its cellular organization is similar to that observed previously in various experimental animals. Cytoplasmic constituents include mitochondria, endoplasmic reticulum, Golgi complex and small filamentous components of low opacity. However, one additional cytoplasmic element has been found solely in the epithelium of cataractous lenses. This appears as an agglomerate consisting of dense granules of varying sizes interposed between larger opaque, homogenous particles of circa mμ diameter. Many epithelial cells contain one or more of these agglomerates in their cytoplasm. They are usually located close to the nuclear membrane and may be surrounded by a pale zone which separates them from the surrounding cytoplasm. In other instances, however, no such boundary can be discerned. This complex resembles a lipofuscin-type of pigment such as that frequently seen in aged human heart muscle. At the present time no comparisons have been made with normal human lenses of similar age, thus a pathognomonic significance of these agglomerates with regard to the senile cataract remains doubtful.

Sensitivity reactions to tuberculin in the eyes of rabbits passively sensitized with leukocytes. Mary M. Tremaine, Ph.D., Department of Microbiology and Immunology, State University of New York Downstate Medical Center, Brooklyn.

In this study, reactions to tuberculin have been investigated by passive cellular sensitization of normal rabbits, using the eye as the indicator system. Under these conditions delayed and immediate-type reactions can be differentiated more clearly than is possible in actively sensitized animals.

An individual experiment was as follows: peritoneal exudative cells (predominantly mononuclear) were collected from four or five rabbits which had been actively sensitized to tubercle bacilli; the cells were pooled and washed once; an aliquot (3 times 10^7) was injected into the anterior chambers of 12 to 14 normal rabbit eyes (local sensitization); another aliquot (1-2 times 10^8) was injected intravenously into another rabbit (systemic sensitization). For tests, dialyzed OT was injected intracorneally into one locally sensitized eye and diluent into another (usually the same animal) at successive intervals of four hours after transfer of cells. Systemically sensitized rabbits were tested in the same way 72 hours after transfer. An eye received only one test. For additional controls, old tuberculin was injected into the corneas of normal and actively sensitized rabbits.

Seven separate transfer experiments have been completed. Of 46 locally sensitized eyes which were tested with old tuberculin, 24 developed corneal reactions. Controls were satisfactory. These reactions in locally sensitized eyes were most frequent and most intense in corneas tested 12 to 20 hours after transfer of cells, indicating that this is the time of maximum reactivity under the conditions of this study. Three corneal reactions of minimal intensity were observed in the seven rabbits that were systemically sensitized. Lack of uniform success can be attributed to the generally low level of sensitivity of donors. Immediate-type reactions (presumed to be due to circulating serum antibody) occurred in three of the seven locally sensitized eyes that were tested at the time of cell transfer. Corneal reactions seemed the same in local and systemic sensitization. They began eight to 16 hours after tests, showing "ground-glass" opacity; reacting eyes also showed circumcorneal injection of vessels, dilatation of vessels in the iris, irregularity of the pupil, and exudate in the anterior chamber (in systemically sensitized animals where it could be seen).

Serial histologic sections of the anterior segment were examined on approximately 50 eyes. Swelling of the cornea was the dominant feature. The entire cornea was swollen in severe reactions; in less intense reactions, the swelling involved the central area and extended to the limbus on one side (rarely, changes were confined to the central portion). Infiltration of the cornea by leukocytes was not intense, but extended over a much greater area (in serial sections) than in controls. Infiltration of cells into the limbus and iris appeared to be inversely proportional to the degree of corneal swelling. Eyes in which the corneal edema extended to one limbus showed the most infiltration on the opposite side. Eyes which had maximal corneal reactions often showed very little infiltration. Antigen may not diffuse to the limbus and iris in this case, or the swelling may constitute a mechanical blockade to cellular infiltration. Infiltrating leukocytes were predominantly mononuclear, and were clustered in perivascular spaces. Free cells were commonly found at the angle and on the posterior surface of the iris.

These results with tuberculin seem essentially identical to those obtained previously using horse serum as antigen (J. Immunol., 79:467, 1957), and support the previous conclusion that delayed-type sensitization is probably a regularly occurring component of the total active response to horse serum. Systemic sensitization by leukocytes with intracorneal tests should be useful in further study of sensitivity reactions in eyes.

Allergic recurrences of toxoplasmic uveitis. Herbert E. Kaufman, M.D., Massachusetts Eye and Ear Infirmary, Boston.

It is known that when an antigen is innoculated into the vitreous, a uveitis occurs which later subsides. This uveitis can be made to recur after the initial intravitreous injection by sys-

temic exposure of the animal to antigen. With the usual soluble antigens, it appears that recurrences are possible until the antigen diffuses out of the vitreous.

Toxoplasmas, being alive and encysting, can persist in the eye for a very long time. After an initial intraocular infection, it seemed likely that any systemic re-exposure to this relatively common antigen might exacerbate the uveitis.

Guinea pigs and rabbits were innoculated intraocularly with Beverly strain Toxoplasmas. As long as one year after the initial infection, exacerbations of uveitis occurred after systemic innoculation of killed organisms. When the intravenous route of innoculation was used, only a minimal uveitis occurred beginning in about two to five hours and disappearing in about 24 hours. When the antigen was injected intraperitoneally and intradermally, however, there was a fulminating uveitis reaching its peak of severity at about 48 hours. In guinea pigs the reaction, though definite, was minimal; in rabbits the inflammatory reaction was obvious and severe. Multiple controls confirmed that this reaction was specific. Histologic studies permitted identification of the organisms in these reacting eyes.

The effects of irradiation and nitrogen mustard on the passive arthus reaction in the rabbit eye. Arthur F. Howe, Ph.D., and S. James Bullington, M.D., Retina Foundation, Boston 14, Massachusetts and Geisinger Memorial Hospital, Danville, Pennsylvania.

Quantitative direct passive Arthus reactions have been produced in the eyes of rabbits treated either with total-body X-irradiation or nitrogen mustard.

In irradiated animals, the reaction was indistinguishable from that produced in unirradiated rabbits, provided the irradiation did not depress the polymorphonuclear neutrophil count to levels below 1000 to 1,500 cells/cu. mm. at the time of initiation of the reaction. With counts below this level, inhibition of the intraocular Arthus reaction resulted, related to the polymorphonuclear neutrophil count rather than to the X-ray dose.

The later stages in the evolution of the Arthus reaction in rabbits which had received total-body irradiation differed from the reaction observed in unirradiated animals by the absence of plasma cells, if the reaction was initiated within two weeks following irradiation.

In nitrogen mustard treated animals with apparent total depletion of the circulating polymorphonuclear neutrophils, it was possible to elicit an Arthus reaction in the eye, but not in the skin, provided sufficient antibody was used. In these rabbits, however, polymorphonuclear neutrophils were observed on smears from the aqueous and vitreous humors. Three mg. antibody nitrogen was necessary to produce a minimal reaction in the eye—a dose five times that required to produce a similar reaction in normal rabbits.

When the circulating polymorphonuclear neutrophils returned to normal in nitrogen mustard-treated animals, the previously negative skin site developed a typical Arthus reaction but there was no exacerbation of the intraocular reaction.

A study of iridocyclitis occurrring in rats with arthritis induced by the injection of Freund's adjuvant. S. J. Bullington, M.D., and Byron H. Waksman, M.D., Retina Foundation, Massachusetts Eye and Ear Infirmary, Boston, the Department of Bacteriology and Immunology, Harvard Medical School, and the Neurology Service, Massachusetts General Hospital, Boston.

A single intradermal injection of Freund's adjuvant was given into the hind foot of a series of rats. After a latent period of 10 to 14 days a high percentage developed a chronic, migratory polyarthritis, subcutaneous ear nodules and much later a dermatitis. About 10 percent of these rats with arthritis developed signs of ocular disease. The ocular involvement appeared to coincide with the development of the concomitant arthritis to its maximum. In a few animals, evidence of a purulent urethritis was also observed. The whole disease complex resembled in some of its manifestations, Reiter's disease in humans.

The gross characteristics of the ocular disease depended on its severity. In mild cases, a conjunctivitis with a few small discrete iris nodules was seen. In the more severely affected eyes there was a white fibrinous exudate filling the anterior chamber, fine keratic precipitates and rarely massive hemorrhage into the anterior chamber. The later formation of posterior synechiae was often observed. A few animals also developed an episcleritis. The ocular disease was not necessarily bilateral.

Histologically, a severely affected eye showed massive infiltration of histocytes and lymphocytes into the ciliary body and iris with many polys in the anterior chamber and posterior chamber. The optic nerve and the retina were never affected and in only one case was there choroidal involvement.

The development of the erythematous indurated eye nodules paralleled closely the onset and time course of the arthritis and the ocular disease (if present). The later dermatosis became only grossly visible at about 35 to 40 days though histologic evidence indicates that the skin lesions were recognized clinically only after its actual onset.

The skin disease was characterized grossly by cracking, scaling, crusting and loss of hair. Histologically, the skin disease and the subcutaneous nodules were quite similar. In mild lesions there were accumulations of round cells in the dermis. In more severe lesions, there was progressively greater invasion of the epidermis by polys with formation of pustules.

The precise etiology and pathogenesis of this experimental disease is not known at present. Arthritis in rats has been described as due to infection with certain organisms. Attempts to culture any organisms in these animals failed. The experimental evidence at present available sug-

gests that the disease process is probably the result of an immunologic reaction produced by some antigenic component of the tuberculosis bacillus. It is felt that this experimental disease may be of considerable interest as a good experimental model for the study of certain categories of human disease.

Osmotic pressure relationship-plasma to aqueous: With special reference to the elasmobranch eye. Russell Doolittle and William Stone, Jr., M.D., Ophthalmic Plastics Laboratory, Massachusetts Eye and Ear Infirmary, Boston, and Marine Biological Laboratory, Woods Hole, Massachusetts.

The elasmobranch eye has been studied because the urea concentration in the plasma is approximately 100 times that in mammalian plasma. It has been found that the same percentage deficit exists in the aqueous of the elasmobranch as in the mammal. There is also a deficit of trimethylamine oxide in the aqueous with no compensating constituents. This produces a hyperosmolarity of the plasma of approximately 25-30 milliosmoles. The calculated difference in the osmolarity based on measured concentrations agrees with freezing point depression measurements made with the Fiske Osmometer. This raises the very interesting question as to whether water is being pumped against a very great osmotic pressure gradient in order to mantain a positive intraocular pressure; namely, are the cells of the ciliary body actively secreting water?

The influence of sanguinarine and argemone oil on the intraocular pressure of cats, rabbits and chickens. G. C. Dobbie, M.D., and Maurice E. Langham, Ph.D., Institute of Ophthalmology, London, England.

The experimental evidence that the glaucoma associated with epidemic dropsy is due to the ingestion of argemone oil has led to a number of studies with sanguinarine, an alkaloid isolated from argemone oil. Several investigators have reported that administration of this alkaloid to animals caused an increased intraocular pressure and recently Hakim (J. Physiol., 138:40, 1957) observed that similar increase in pressure could be induced by very small amounts of the drug injected directly into the lateral ventricle. Furthermore, he reported that daily intraventricular injections of the drug induced a chronic ocular hypertension in cats. In the present study the mechanism of these changes has been investigated.

The effect of sanguinarine on blood and intraocular pressures in rabbits and cats was assessed using a manometric technique. An intravenous injection of 1.0 to 4.0 mg./kg. of sanguinarine chloride or nitrate caused a concurrent rise in blood and intraocular pressures; both pressures returned to normal within 10 to 20 minutes. Higher doses caused a variable effect on the blood and intraocular pressures but again the time course and nature of the changes in the eye and blood were the same.

In similar experiments, attempts were made to induce a change in the steady-state pressure of the eye by a slow intravenous infusion of sanguinarine (0.4 to 1.0 mg./kg./min.). Under these conditions no changes in blood or intraocular pressures were observed over infusion periods of 20 minutes. Furthermore, in conscious rabbits given an intravenous injection of 2.0 mg./kg. of sanguinarine every 30 minutes no increase in the equilibrium pressure in the eye was observed.

Injections of 10 to 100γ of sanguinarine into the lateral ventricles of rabbits and cats caused a concurrent rise in the blood and intraocular pressures. In the same animals 1000γ of sanguinarine injected intravenously caused no change in the blood and intraocular pressures. Conscious cats were injected intraventricularly with sanguinarine once daily for periods up to 40 days without producing a chronic ocular hypertension. In these experiments cats were found to tolerate approximately 50 to 70γ of sanguinarine daily but higher doses proved fatal.

Feeding of sanguinarine to rabbits, cats and chickens for experimental periods up to 40 days caused no ocular hypertension. Hens were found to tolerate without loss of body weight over 100 mg. sanguinarine daily and continued to lay eggs; sanguinarine was readily detectable in these eggs.

In a final series of experiments, argemone oil was fed daily to chickens. Under these conditions feeding of as little as 5.0 ml. of argemone oil caused edematous changes in their combs and wattles.

These experimental results failed to confirm the reports of previous investigators that sanguinarine could produce a chronic hypertension in animal eyes and suggest that sanguinarine is not the agent responsible for the edema and glaucoma associated with epidemic dropsy.

Comparative anatomy of the ciliary nerves. Patricia Grimes, B.A., and Ludwig von Sallmann, M.D., Ophthalmology Branch, National Institutes of Health, Bethesda, Maryland.

Recent studies in the field of ocular physiology have shown that a detailed knowledge of the anatomy of the ciliary nerves in different species of experimental animals is required for effective pursuit of experimental procedures. Such knowledge is necessary particularly with respect to interconnections of sympathetic, parasympathetic and sensory supplies. In the present work the distribution of these nerves has been investigated by dissection of the orbital contents of a large number of rabbits, cats and monkeys. A smaller number of human preparations were also dissected. Christensen's silver staining technique was modified to yield light stable preparations. This facilitated the isolation and the photographic recording of even fine branches of the selectively stained nerves.

Comparison of the ciliary nerves in the experimental species showed a basic pattern common to all, but variations from species to species were

striking. The greatest differences were in the size and accessibility of the ciliary ganglion and in the degree of fusion of the sympathetic and sensory nerves with the ciliary ganglion or the postganglionic branches. These observations have been helpful in studying afferent impulses and the effects of electric stimulations of such nerve branches on the intraocular pressure.

Histochemical localization of cholinesterase in human extraocular muscle. Carl Kupfer, M.D., Howe Laboratory, Harvard Medical School and the Massachusetts Eye and Ear Infirmary, Boston.

Using a modification of the Koelle-Friedenwald histochemical technique for the localization of cholinesterase, 25μ thick sections of human extraocular muscle were stained. The distribution of typical motor end plates was noted. It appears that there is more than one end plate in each extrafusal muscle fiber, the usual number appearing to be two. In some fibers, three and four end plates were noted. In fewer number of fibers, only one end plate was present. The physiologic implications of this finding are discussed.

Experimental diabetic retinopathy. Andrew de Roetth, Jr., M.D., Columbia University, College of Physicians and Surgeons, New York.

Alloxan diabetes was produced in young male albino rats. At monthly intervals the animals were killed, the retinas were dissected and their metabolism studied in vitro employing Warburg manometric techniques. A decided difference was found in the rates of anaerobic glycolysis of the retinas of the diabetic animals as compared to the retinas from the normal rats. Other metabolic differences were also observed between the normal and the diabetic animals and the hypothesis is presented to explain these biochemical changes.

Herpes simplex virus inactivation by chemical agents. Theodore W. Sery, Ph.D., and Francis P. Furgiuele, M.D., Wills Eye Hospital, Department of Research, University of Pennsylvania Graduate School of Medicine and Temple University, Philadelphia.

Many chemical compounds of synthetic and biologic origin have been studied in recent years in various laboratories in an attempt to find agents that would be virucidal, virustatic or which would be able to interfere with the host cell's virus-duplicating process.

In this work a number of these compounds as well as a host of other chemicals have been tested against herpes simplex to determine whether any new effective chemotherapeutic agent may be available for dendritic keratitis.

An in vitro technique was used for screening the various agents for possible strong virus inactivating properties and the most promising among these were then tested against herpes infections of the rabbit cornea. Criteria for the latter tests were based on the ability of a given agent to prevent the formation of dendritic figures on the cornea after administering an inoculum in the range of two million virus particles. Therapy was started only one hour after inoculation and repeated daily for one hour intervals. The screening procedure was done quantitatively on embryonated chicken eggs and a strong antiviral property was attributed to a given agent if it totally inactivated a given viral inoculum at concentrations of 10^{-3} molar or less. The results of the in vitro screening tests revealed a number of highly active antiviral agents. Some of these were agents with known virus inactivating properties such as sodium desoxycholate, Zephiran, Sod. lauryl sulfate, p-chloromercurisodium benzoate and ascorbic acid. The quantitative data on these compounds served as a comparative guide for all other agents tested.

Aside from a large group of agents that were relatively inert, a few new agents were revealed to be extremely potent in vitro due to their ability to totally inactivate virus at unusually low concentrations such as 10^{-4} and 10^{-5} molar. A study of 30 metallic cations showed only a small number of heavy metals in a fairly well-circumscribed portion of the periodic table of elements to be strongly antiviral. The most active of these were the silver, mercuric and uranyl ions. Others almost as active were bismuth, cadmium gold and palladium. Silver and mercury gave total virus inactivation at 10^{-5} molar concentration. This molecular concentration for the silver ion, as a solution of silver nitrate, amounts to 1.7 μg./ml. or 0.00017 percent. Extensive in vivo trials with silver and less extensive tests with the other cations were of no value in herpetic keratitis in the rabbit. Silver nitrate may yet be of value in conjunction with mechanical cauterization of human corneal infections. The silver ion is at least 100 times more virucidal than iodine which is a commonly used cautery agent for herpetic keratitis. The possible value of silver nitrate will have to await clinical trials.

A second group of highly active agents were members of the p-benzoquinone family of chemicals. Many of this series that were tested were virucidal at low concentrations of 10^{-5} molar; in the case of p-benzoquinone this amounted to 1.0 μg./ml. which lies in the range of antibiotic concentrations. The great number of derivatives of quinone, naphthaquinone and anthraquinone that occur in nature provide a broad area for further research in the quest of an agent suitable for viral therapy. Many of the agents of this group that were tested were highly toxic to the cornea but some derivatives such as chloranil, and quinizarin were very safe and could even be dusted directly on the rabbit cornea with no untoward effects. The lack of in vitro activity of such compounds remains but they provide a new and extensive source of natural and synthetic antiviral compounds for further study.

The distribution of mast cells in the uvea. George K. Smelser, Ph.D., and Steven Silver, B.S., Departments of Anatomy and Ophthalmology, College of Physicians and Surgeons, Columbia University, New York.

By means of suitable incisions the sclera and attached choroid and pigment epithelium of albino guinea pigs, can be prepared as flat whole mounts. Similar preparations can be made of the iris and ciliary body. When these are stained with toluidine blue in a highly acidic solution (0.5 percent HCl), practically nothing is colored other than the granules of mast cells. Such preparations allow one to determine the number and distribution of mast cells in these and other thin membranes. Since these cells were not found in the sclera and since the retina was readily removed, the mast cells seen were restricted to the uveal tract. Very great concentration of these cells was found in the posterior portion of the choroid and adjacent to the long posterior ciliary artery. Their concentration there was 10 to 20 times that seen in other connective tissue membranes. Mast cells in the choroid just posterior to the ora serrata were much less densely distributed being no greater in number than those found in peritoneal mesenteries, pericardium or kidney capsule. Mast cells were numerous in the ciliary processes but almost absent from the iris stroma. Good evidence links the mast cell with the production or storage of such physiologically active compounds as heparin, histamine and serotonin. The physiologic significance of the striking distribution pattern and high concentration of these cells in the guinea pig uvea is unknown.

A study of rod activity at protopic intensity levels. Joseph Mandelbaum, M.D., and Elliot Nelson, M.D., New York State University, New York.

It was the purpose of this investigation to study the extent of rod activity at photopic levels of illumination. The method was to compare the apparent saturations of colored lights of low photopic intensities as viewed by the two eyes, one of which had previously been light adapted and the other dark adapted. To the light adapted eye, where there was presumably little if any rod activity, the color appeared quite saturated. To the dark adapted eye, with near maximal rod function, the color appeared pale, unsaturated. This difference was attributed to rod activity. An attempt was made to study this effect quantitively by means of a specially constructed color mixture apparatus. White light was added to the colored light viewed by the previously light adapted eye in order to match the degree of desaturation as observed by the dark adapted eye. The amount of white light was taken as an index of rod activity at the intensity level being studied. Measurements were made at intensity levels from about 10 times the cone threshold to 10,000 times in steps of one log unit. Violet, green and red lights were provided by appropriate narrow beam filters. In the intensity range between the cone threshold and 10 times the cone threshold the predominance of rod activity was so great that measurements could not be made, the colored light appearing completely desaturated. At 10 times the cone threshold (7.2 log micromicrolamberts) rod activity was still very strong, contributing from four to 16 times as much as the cones to total brightness sensation. At 100 times the cone threshold the rods were still two to seven times as effective as the cones. At 1,000 times the cone threshold rods and cones seemed to be equally effective. At 10,000 times the cone threshold (10.2 log micromicrolamberts) the cones predominated completely, and rod activity was no longer significant. This effect was evident for all colors studied, despite the difference in their photochromatic intervals.

Distance lateral heterophoria and the response AC/A ratio and their relationship to the elevation of the plane of regard. Henry A. Knoll, Ph.D., Bausch & Lomb Optical Company, Rochester, New York.

It is often stated that the lateral heterophoria varies with changes in the elevation of the plane of regard. Exophoria increases (esophoria decreases) with upward gaze, exophoria decreases (esophoria increases) with downward gaze. The statement seems to apply to the near phoria, although this is not always specifically stated.

These changes in the near phoria can be explained in several ways. If accommodative response is not carefully controlled, then the increase in esophoria with downward gaze could be explained by a higher accommodative response. It is my opinion that this is the explanation for the clinically observed facts. It would also explain laboratory findings where the accommodative response is not measured.

If the anisophoria is real and not apparent, then there are several possible explanations. One is that the distance phoria is independent of the elevation of the plane of regard and the response AC/A increases with decreased elevation. A second is that the distance phoria changes with elevation of the plane of regard and that the response AC/A ratio is constant. Thirdly, both the distance phoria and the response AC/A may remain constant, but the proximal convergence may vary.

Data are presented which indicate that anisophoria, associated with elevation of the plane of regard, is more apparent than real.

The influence of retinal adaptation upon the pupillary reflex to light in normal man: II. Effect of adaptation to low-intensity illumination upon pupillary reactions to bright light. Otto Lowenstein, M. D. and Irene E. Loewenfeld, Ph.D., Columbia University, College of Physicians and Surgeons, New York.

In previous work on the relations between visual perception and pupillary activity, the effect of adaptation to bright white or red light upon the pupillary threshold was determined. (Am. J. Ophth. **48**:536, 1959). The present study deals with the reverse experimental conditions, that is, the effects of adaptation to dim light upon pupillary reflexes elicited by bright light. These effects will be discussed in terms of their probable mechanism and neuroanatomic localization.

SOCIETY PROCEEDINGS

Edited by Donald J. Lyle, M.D.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

447th meeting, February 18, 1959

Henry L. Birge, M.D., *presiding*

Hemorrhagic glaucoma: the diagnostic trap

Dr. Irwin T. Mancall, Hartford, Connecticut: Few clinical entities in ophthalmology art as clear cut and as well defined as hemorrhagic glaucoma. This disease, most commonly occurring after occlusion of the central retinal vein, makes its appearance from two weeks to three to four years after a vascular accident, although usually within one year. The story of such cases is a familiar one: the patient, with a previous history of sudden loss of vision in one eye, complains of pain in that eye, with headache, perhaps nausea and vomiting. He is found to have severe conjunctival injection, bullous keratopathy, a deep anterior chamber, fixed pupil, and an iris covered with new-formed vessels. If the fundus is visible, hemorrhages are to be seen scattered throughout the retina. The tension is high and the diagnosis is obvious. Often the eye is enucleated because of intolerable pain.

Not all cases of unilateral glaucoma with high tension following central retinal vein occlusion are, however, hemorrhagic glaucoma. Since some of these eyes may be saved and wind up with useful vision, the problem of diagnosis and management is more than academic. Furthermore, providing it is certain that a tumor does not exist, a blind but comfortable eye is preferable to a prosthesis.

This can be illustrated by four cases, of unilateral glaucoma following occlusion of the central retinal vein. All of these cases had many of the features of hemorrhagic glaucoma.

One of these turned out to be secondary glaucoma following iridocyclitis and another was due to mechanical obstruction of the angle by blood pigment. One of the remaining two was hemorrhagic glaucoma in which broad peripheral anterior synechias preceded the appearance of neovascularization by two months. The last case had no visible vessels at the time of enucleation, although these were present in microscopic sections.

These findings suggest that, clinically, the diagnosis of hemorrhagic glaucoma can be made on the basis of broad peripheral anterior synechias which precede the appearance of new vessels on the iris and angle, although these vessels are undoubtedly present from the onset.

Roentgenographic diagnosis of lacrimal gland tumors

Dr. Alexander S. MacMillan, Jr., Boston: In performing X-ray examinations for lacrimal gland tumors the first and most obvious finding is that we see nothing. The next possible finding, and this is nonspecific, is that of generalized increased density in the orbit. This increased density is not bony; it is soft tissue. Another nonspecific finding is a generalized increase in the size of the orbit, as reported by Ingalls.

One of the most reliable and specific findings is that of enlargement of the lacrimal fossa. Also the orbital rim often becomes dense and sclerotic. One of the more specific and lethal findings is the presence of malignant bone invasion. Another finding is that of calcification.

Here at the Massachusetts Eye and Ear Infirmary we have had, in a period of 20 years, 11 completely documented cases of lacrimal gland tumors. This means that in our hospital the tumor is not a common one and that we have not had the opportunity to gain a great deal of experience.

Two of these 11 lacrimal gland tumors showed nothing on X-ray examination. Eight of them showed increased density within the orbit—increased soft tissue density and loss of the periorbital fat radiolucency. We did not see any generalized increase in the size of the orbit in any of the cases.

Four of the cases showed localized lacrimal fossa enlargement. Two of these showed associated sclerosis in the orbital region. Four of the cases showed bony invasion at first and in two of these the disease later spread.

Here is an incomplete pathologic evaluation of these cases: Four were undifferentiated tumors; one was a grade-3 adenocarcinoma; one was termed a low-grade adenocarcinoma; one an epithelioma; and four were termed mixed tumors.

Five of these patients with lacrimal gland tumors have died. Their cases were of the undifferentiated adenocarcinomas and mixed tumor varities. This series is much too small for statistical evaluation. X-ray examination appeared to be of diagnostic value in roughly 50 percent of our cases. X-ray therapy was only used for palliative purposes in cases with bone invasion.

Pathology and prognosis of epithelial tumors of lacrimal gland

Dr. Lorenz E. Zimmerman, Washington, D.C.: I find myself in disagreement with statements made by others concerning tumors of the lacrimal gland. The first major point of disagreement concerns the often-repeated statement that 90 percent of lacrimal tumors are mixed tumors. Closely related to this is the second statement that mixed tumors of the lacrimal gland have a very poor prognosis. And, third, we are told that mixed tumors because of their poor prognosis should be treated by exenteration.

What is the true incidence of mixed tumors of the lacrimal gland? A good answer to this question has been provided by Reese. Here you find that roughly 30 percent are inflammatory and another 20 percent are in the lymphoid group. In other words 50 percent of the tumors present in the lacrimal fossa are tumors that should not be treated surgically. Now this leaves us with 50 percent of the tumors and these are epithelial tumors and of this 50 percent about half are mixed or other benign tumors and half are carcinomas.

It is often said that we see the same epithelial tumors in the lacrimal gland as in the salivary gland. With a few reservations this is true. The most important difference is the greater proportion of malignant tumors in the lacrimal gland and especially the frequency with which adenoid cystic carcinomas are encountered in the lacrimal gland. In the salivary gland not only are the benign mixed tumors more common but there are other benign tumors that we do not see or rarely see in the lacrimal gland.

Investigators of recent times have emphasized the fact that benign mixed tumors if removed completely with the capsule intact should not be expected to recur or metastasize.

In my review of tumors of the lacrimal gland I have found that the following simple classification is useful: There are two main groups (1) those tumors that are related to mixed tumors and (2) those tumors that are not related to mixed tumors.

Most of the mixed tumors are perfectly benign. These benign mixed tumors account for about 45 percent of the epithelial tumors of the lacrimal gland. Grossly one of these tumors presents a single multilobulated mass which appears to be encapsulated. It is important to examine the gross specimen very carefully and look for areas where the capsule is broken, for areas of hemorrhagic necrosis, and areas of softening. These are the areas that are most likely to give rise to or contain areas that have undergone malignant change.

Current histopathologic classification of tumors of the lacrimal gland is of clinical value in that it provides prognostic data and indicates appropriate therapy. Benign mixed tumors of the lacrimal gland should be excised in a block dissection with the periosteum of the lacrimal fossa attached.

On the other hand, I think that exenteration is unnecessarily radical for the benign mixed tumor. But malignant epithelial tumors of all types are best treated by exenteration plus resection of invaded orbital bones and removal of the supraorbital nerve.

Charles Snyder,
Recorder.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

Section on Ophthalmology

March 19, 1959

Harold G. Scheie, M.D., *Chairman*

Angiomatosis retinae

Dr. David Seaman (by invitation), in reporting two operated cases, said that angiomatosis retinae is characterized by a pair of grossly enlarged blood vessels which course from the disc to the retinal periphery and terminate in an elevated circumscribed tumor. Throughout the retina are scattered collections of lipoidal vascular exudates. There have been 175 cases reported in the literature.

In two patients, aged four and 20 years, recently operated at Temple University Medical Center, the angiomas were unioocular. In neither case was there any evidence of central nervous system or general systemic involvement.

In each case the sclera was exposed over the tumor site and penetrating micropins were placed into the tumor. Several applications of diathermy coagulation were employed using a current of 40 ma. for eight seconds per application over the tumor area. No intraocular hemorrhage occurred.

The appearance of the tumor did not change immediately following diathermy but, subsequently, the angiomas became much smaller in circumference and showed a 50-percent decrease in elevation. A follow-up study is planned to determine the necessity of further therapy and to watch for development of additional angiomas.

Management of patient with subnormal vision

Dr. Bernard C. Gettes: In December, 1955, a low-vision clinic was established at the Wills Hospital. Since that time, 285 patients have been seen in consultation. These examinations showed:

1. One can prognosticate which patients are suitable candidates for a visual aid. This is based on: (a) proper motivation; (b) visual acuity of at least 20/500; (c) an adequate peripheral field.

2. Selection of the applicant is based on the patient's visual acuity which was tested in many ways: (1) Stimson target test charts, (2) Keeler near charts, (3) Sloane near charts, and (4) Lebensohn test charts. The last three charts were evaluated and found to be comparable in their purpose. The method of testing is not difficult. The Stimson charts appear to be the easiest to utilize from the standpoint of the patient and the examiner.

3. Testing and examination of the patients does not require a special clinic, nor does it necessitate expensive equipment.

Corticosteroids in herpes zoster ophthalmicus

Dr. Harold G. Scheie and Dr. Thomas G. McLellan, Jr., (by invitation) summarized the results of treatment of 25 cases of herpes zoster ophthalmicus, all with intraocular involvement. The usual initial dose of corticotropin was 40 units intravenously in an eight-hour infusion. When progressive improvement had occurred, intramuscular therapy was substituted; and a few days before parenteral therapy was stopped oral corticosteroids were started in standard doses. Pain was usually relieved within 48 hours of starting therapy. Ciliary flush decreased after the first day of therapy. Clearing of the aqueous was noted. Clearing of the aqueous began in 48 to 96 hours. Six patients had recurrent iridocyclitis after the initial attack had subsided and all medications had been stopped. Recurrences were readily controlled by resuming oral corticosteroid therapy.

In a total series of 36 patients so treated two have shown significant visual loss. Thirty-four have retained normal vision. The authors believe that at present systemic corticotropin and corticosteroids are the treatment of choice for herpes zoster ophthalmicus.

William E. Krewson, 3rd,
Clerk.

MADRID OPHTHALMOLOGICAL SOCIETY

April 21, 1959

DR. MARIN AMAT, *presiding*

CONGENITAL EDEMA OF DISC

DR. PÉREZ LLORCA presented a case of a boy, eight years of age, who complained of headaches. On examination the right eye had a myopia of 4.0D. and emmetropia, O.S. Normal vision was obtained, O.U. Bilateral papilledema was present. Fields, and complementary examinations were negative. For four years the discs have remained the same.

Dr. Pérez Llorca believes the case to be a congenital edema of the disc.

Discussion. DR. LEOZ DE LA FUENTE described a similar case in a boy, aged nine years, who also has had no change of the discs.

DR. MARIO ESTEBAN pointed out that the lack of venous pulse in this case eliminates the possibility of intracranial hypertension.

DR. JIMÉNEZ JORDAN brought out the possibility of a protein disturbance in chilhood that could have produced a greater absorption of water at the disc.

DR. BARTOLOZZI AND DR. MARIN AMAT favored congenital anomaly. The latter mentioned various examples of hypermetropia in children who in spite of becoming emmetropes later continued to show edema of the disc. The case of a boy, son of a luetic, in whom even after specific treatment no variation of the disc's appearance was noted, was described.

ORBITAL TUMORS

DR. PÉREZ LLORCA commented upon four cases of orbital tumors, three of which were operated by an anterior approach: one a myxoma, another a cavernous angioma, and the third an epithelioma.

The cavernous angioma oddly was accompanied by a nonreducible exophthalmos. It was excised in toto.

The epithelioma, although excised, has reappeared.

The myxoma was clinically diagnosed. The tumor surrounded the optic nerve which was excised together with the neoplasm. The eye remained with normal movements and amaurotic. The orbital myxoma is a rare finding. The confirmation of this case awaits pathologic diagnosis.

Dr. Pérez Llorca also presented a boy, aged 14 years, with an intermittent exophthalmos of the right eye, which increased with exercise and by bringing the head down. Dr. Llorca, explained in detail his preference for the anterior access of the orbit dissecting through orbital tissue instead of the lateral approach with the Krönlein method or the transfrontal. In the cases where this practice cannot be followed because of deeply placed tumors he urges cooperation between the ophthalmologist and the neurosurgeon.

Discussion. DR. LEOZ DE LA FUENTE mentioned three cases of orbital tumor. One an angioma of the sheaths of the optic nerve excised through an anterior approach; another an angioma of the optic-nerve sheaths, the size of an eye, which Dr. Obrador took out transfrontally; the third case was in a girl, the eye being enucleated years before because of a glioma which was now recurring.

DR. ARJONA mentioned a patient of his, whose eye was enucleated 14 years before because of a choroidal sarcoma, who had a recurrence in the orbit.

DR. MARIN AMAT explained that cavernous angiomas of the orbit and of the lids are usually encapsulated and therefore are easily excised, while the simple angiomas are not so limited.

INTRAOCULAR FOREIGN BODY

DR. MORENO CASANOVAS presented a case of intraocular foreign body. A young lady consulted because of diminution of vision of the right eye. The history was negative. On ophthalmoscopic examination a whitish exudate at the inferotemporal quadrant of the retina was seen. The vision was 1/6 and a presumptive diagnosis of cysticercus was made.

Insisting on the history the patient re-

membered of having had a blow on the eye. The X-ray films demonstrated an intraocular foreign body. Today the fundus showed at the site of the whitish exudate, a heavily pigmented retinal plaque.

Discussion. Dr. Arjona has seen retinal pigmentation appear in cases of intraocular foreign body seven days after the accident. Also he does not consider that siderosis oculi always brings a negative visual prognosis and cites a case of a woman with siderosis and cataract upon whom he operated, and obtained vision of 1.0.

Dr. Soto Faure described the case of an office employee with an orbital tumor that turned out to be a small stone weighing 0.25 gm.

Dr. Pérez Llorca favors early surgery in intraocular foreign bodies except in the case of multiple shots or of well-tolerated foreign bodies in the vitreous, such as glass. He recommended removal of magnetic foreign bodies through a posterior approach.

Dr. Mario Estéban recommended early extraction of the foreign body in spite of the fact that there may be cases of siderosis in which vision may be preserved. He prefers a posterior approach preceded by scleral diathermy at the place of the incision.

Obliteration of lacrimal canaliculi

Dr. Wellington Amaya presented a case of partial obliteration of the lacrimal canaliculi in a 15-year-old girl. Ten years before she had suffered arsenic intoxication and pemphigoid lesions appeared at the internal canthus of both eyes, causing symblepharon between the superior and the inferior canaliculi with obstruction demonstrable at exploration. Both probing and the use of a polyethylene tube failed, and future therapeutic measures must be considered.

Dr. Gómez Liano recommended suturing the conjunctiva to the lacrimal sac mucosa, thus diverting the tears toward the nasolacrimal duct. If desired, the connection could be kept patent by a polyethylene tube surrounded by mucosa.

Dr. Leoz de la Fuente considered that the most difficult problem of lacrimal obstructions are those where the canaliculi are involved.

Dr. Pérez Llorca suggested that since permanent placement of a polyethylene tube has already failed it might be possible to open the canaliculi freely, place the tube and, with it in place, reconstruct the canaliculi.

Dr. Marin Amat said he has had very poor results with canaliculi obstructions but he had noticed through the years that there is no need to be worried about the meticulous integrity of the inferior canaliculi when probing, since many patients with total debridement of the inferior canaliculius present no tearing. He advised Dr. Pérez Llorca to perform an ample dilation of the inferior canaliculus up and back, carrying it past the obstruction, trying to keep it patent.

Lens foreign body

Dr. Sastre discussed the policy to follow with a foreign body in the lens. His patient showed a small particle of iron in the lens, which has remained transparent. The visual acuity is 1.0. Dr. Sastre recommends surgery if the opacity progresses. The foreign body can be removed and then depending on the condition of the lens, extraction can be decided on. The lens, being of ectodermal origin, tolerates foreign bodies fairly well.

Rare foreign body

Dr. Rodriguez Montes presented a case of a rare foreign body. A small tumor, the size of a chestnut, was found in the left orbit at the superonasal angle. Some physicians believed the lesion to be an encephalocele; others a dependency from the frontal sinus. Negative X-ray films discarded this last possibility. The pathologic study reported the lesion to be granulation tissue infiltrated with hemosiderin and giant cells; that is, a granuloma secondary to a foreign body with hemorrhage.

Olga Ferrer,
Translator.

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FIRST CONGESS OF THE EUROPEAN SOCIETY OF OPHTHALMOLOGY

The First Congress of the European Society of Ophthalmology, recently formed with the blessing of the International Council of Ophthalmology, was held in Athens, Greece, from the 18th through the 22nd of April, 1960. More than two thousand members and guests from about 40 countries were present. Approximately thirty ophthalmologists and their wives from the U.S.A. were there too. The brilliantly lucid spring sunshine, for which Greece is noted; the surrounding aura of classical history; the pure Grecian architecture of the buildings of the Polytechnical School, where the meetings took place; the high patronage of Their Majesties, the King and Queen of Greece; the generous and most gracious hospitality of

the local hosts created a many splendored background.

The colorful and moving opening ceremonies were held on the morning of April 18th in the Palace Theater. Upon the stage, semicircled with plants and the flags of all nations and in front of a blown-up replica of the official badge of the Congress sat the officers and members of the International Council, members of the Council of the European Society, members of the Committee of Honor consisting of various ministers, diplomats, rectors, and deans of the universities of Greece; the Mayor of Athens; the president of the Academy and officers of the local National Committee, the president of which is the distinguished Professor Jean Charamis. The multicolored academic hoods, gowns, and decorations worn by these distinguished people represented world famous universities and colleges from every part of Europe. It all formed an unforgettable and most impressive picture.

After the arrival of the Royal Party, Prof. Charamis officially opened the Congress with an eloquent speech of gratitude to the King and Queen for their patronage; to the ministers of the Greek government for their aid and a message of friendship and welcome to the members and guests. He pointed out the great debt that Western Culture owed to ancient Greek civilization, particularly medicine. Among other stirring remarks he said, "We are happy to welcome you who are attending our Congress to this country which has been the cradle of light and serenity. Illustrious Athens, Greece of Greece, the divine city welcomes you to the foot of the sacred rock, the Acropolis, which radiates the immortal Greek Spirit which succeeded in founding the eternal laws of truth, of beauty, of good and has produced unequaled masterpieces and eternal models of expression and art. . . . Throughout the work of this Congress, turn your eyes to the Parthenon, dwelling place of the Goddess of Wisdom, whose spirit has been an inexhaustible source of civilization. The temple of the Wingless Victory, jewel of the sacred rock, rises here, a precious symbol in marble. Its sight will inspire you with strength and hope. Remember that it was here, after Marathon, that Nike, companion of Pallas-Athena, laid down her wings and loosed her sandals, having chosen this city, which today welcomes you, as the home of her everlasting stay."

King Paul then declared the Congress to be open and told the delegates and guests in impeccable English that, "Sometime ago my own sight was saved, thanks to your science and understanding." The King, who had had a successful cataract operation a year before, added, "I believe that in a union of knowledge and human kindness lies the solution to many of our contemporary problems, not only of health, but also of politics, economic and human relations." After warmly welcoming the delegates, he added, "I know that you are not only distinguished scientists, but also great philanthropists who, in your service to mankind, combine your knowledge with human sympathy. Very often our sympathy for the sick leads us to forget the pain and agony felt by doctors in the fight to save their patients.

"I wish you to know that I, personally, appreciate fully the outstanding importance of modern medical practitioners, and that I consider them as an example of what might be achieved if only we learned to apply your high standards of values to our everyday life.

"Most of you must have studied the Concept of Ancient Greece. Your presence here is in itself a tribute to the Spirit of Science as it was sprung from the mind of our ancestors.

"But your presence is also a tribute to Contemporary Greece, the country in which, through the ages of ordeal, a spirit of human solidarity and understanding has been cultivated, a spirit with which you will come face to face in all your steps.

"It is the same spirit that my wife and myself have palpable examples in our daily life, through our people, and this realization renders us the happiest people in the world.

"Whenever you see a man, a woman, or a child smiling at you, please remember that the smile is not merely a sign of affability towards you as our guests, but rather a smile of triumph over their misery; in fact, their smile is offered rather as a benevolent blessing to you as their fellow men.

"I know that you will be received well by my people everywhere. I also know that as long as human kindness is kept alive in our hearts, God's blessing will touch our hands irrespective of whether we are laborers, kings, rich, poor, or simple men or doctors."

Following this noble address, the Minister to the Prime Minister, Constantine Tsatsos, spoke. He emphasized the contribution of ancient Greek science to modern scientific progress. He said that Greek medical science helped to dispel deep-rooted prejudice and occult practices and to lay the foundations of modern medical treatment. He added that the present Congress is a tribute to ancient Greek science, and above all, to Hippocrates, the father of medical science, who was the first to preach moderation.

Then followed short addresses by Sir Stewart Duke-Elder, president of the International Council; by the secretary general of the European Ophthalmological Society, Prof. Jules François, whose extraordinary skill of organization played a most important part in making this Congress one of the most successful and efficiently run that I have ever attended; Prof. J. Boeck (Austria); Dr. J. Sedan (France); Prof. Mrs. Radnót (Hungary); Dr. P. Riise (Norway); and by Dr. N. Ayberk (Turkey). The final address was by Prof. Mrs. Muchoskayia of Odessa, U.S.S.R., who spoke in Russian, no doubt on orders but contrary to the rule of the Congress that specified that the official languages were to be French, German, and English. This boorish discourtesy was somewhat softened by her concluding with a few felicitious phrases in good English.

The official badge of the Congress consisted of a handsome bronze medal about the size of a silver dollar, on the face of which was a reproduction of a famous fresco of the abduction of Europa by Zeus in the form of a bull, by E. Kelaidis, well-known modern Greek sculptor. On the obverse sides the words, in Greek, "First Congress of the Ophthalmological Society of Europe. Athens —1960." The medal was suspended by ribbons of different colors signifying officers, members, associates, and so forth, as the case might be.

The scientific work of the Congress then proceeded simultaneously in two auditoriums. In one of these excellent simultaneous translations (through individual transistors) in the three official languages were offered. The official subject for discussions dealt with "Secondary glaucoma," and the subject was faithfully adhered to even in the "free papers" division.

It is impossible to give here more than a list of the titles of the official reports and their authors. Every possible aspect of the subject was covered, and the printed transactions will disclose a wealth of important knowledge presented by world authorities. We shall look forward with eagerness to the appearance of these transactions.

Excerpta Medica (The International Medical Abstracting Service) had gone to great trouble in printing abstracts of all of the papers in English, French and German. Unfortunately my copy was not available to me in time to be of help. However, it could have been of great service in helping one to pick and choose the papers he wished to hear.

The titles and names of the authors follow. Secondary glaucoma due to (1) Uveitis (R. Weekers of Belgium); (2) Lenticular intumescence or displacement of the lens (S. Miller of Great Britain; (3) Postoperative glaucoma (Jayle and Ourgaud of France); (4) Progressive essential atrophy of the iris (S. Miron and A. Willentz of Roumania); (5) Hemorrhage of the anterior or posterior segment (Werner of Ireland); (6) Exfoliation of lens capsule (Joannides, Katsourakis and Velissaropoulos of Greece); (7) Pigmentary glaucoma (Cavka of Yugoslavia);

(8) Epithelial or endothelial proliferation in the anterior chamber (Thiel of Germany); (9) Seclusion of the pupil (Moreu of Spain); (10) Obstruction of extraocular veins (Pulsating exophthalmos, obstruction of venae vorticosae, orbital tumors, obstruction of the superior vena cava vein) (Bietti of Italy); (11) Thyrotropic exophthalmos (Boeck of Austria); (12) Thrombosis of central vein of the retina. (S. Vannas of Finland); (13) Rubeosis irides (Ohrt of Denmark); (14) Trauma (Heinc of Czechoslovakia); (15) Intraocular tumors (Papolczy of Hungary) and (16) Heterochromia irides of Fuchs (Huber of Switzerland). There were approximately 38 free papers covering varying aspects and opinions on the subject of secondary glaucoma.

In adjacent halls there was a scientific exhibition, containing 11 excellent presentations and also extensive commercial exhibits by firms from everywhere in Europe and England as well as three from the U.S.A. These exhibition halls were always crowded with members seeking to uncover the latest in scientific instruments and equipment.

Films, mostly of a surgical nature, were projected each day in a fine and roomy amphitheater. On the whole, they were quite good, most of them in color and about half with sound. The author of each film was usually present to interpolate his remarks into a loud speaker.

Also, scattered throughout the busy schedule, separate meetings of the following groups were held: the International Society of Clinical Electroretinography; Executive Committee of the International Association for Prevention of Blindness; International Professional Association of Oculists; International Organization against Trachoma and the European Group on the Study of Strabismus. In addition there was a round table discussion on the use of alpha chymotrypsin under the chairmanship of Arruga of Spain. J. Barraquer opened the discussion with a prepared paper covering all aspects of the use of alpha chymotrypsin, following which members of the panel, consisting of experts from every part of Europe, entered into a lively debate, mostly in French, which I regret to say I could not follow too well. Castroviejo and Olga Ferrer very kindly did some interpretation and summaries in English for those of us who knew little or no spoken French. It was interesting to note that most of the experts were in accord with the report presented at the American Academy of Ophthalmology and Otolaryngology last year. A note of conservatism was most evident. The members of the panel were in almost unanimous agreement with Arruga's summary at the end. The conclusions were that the use of the enzyme in patients under 10 was almost always disastrous and should be condemned. In patients between the ages of 10 to 20 years its use was difficult and dangerous, in patients aged between 20 and 50 years its use was most valuable and important and after 50 years of age it was often unnecessary. There was evident a strong feeling against its use in cases of high myopia (particularly by François and Castroviejo) due to the increased incidence of retinal detachment that had been noted. Recordings were made of the discussion and it is hoped that after editing, these will be incorporated in the transactions.

The social events formed an unforgettable impression of beauty, charm, and great warmth of hospitality. The Greek government gave a magnificent reception to all members and guests on the first evening. On the next evening there was a superb and professional performance of "Oedipus-Rex" (Sophocles) in the Royal Theater. The staging, lighting, and chorus were extraordinarily good. The acting by the principals was smooth and inspired. The costuming was charmingly classic. The National Committee gave a glittering reception followed by folk dancing and a ball at the King's Palace Hotel the next night. On the final evening, April 21st, the official banquet at the Grande Bre-

tagne Hotel took place. Following a Lucullan feast, exquisitely served, speeches and toasts were given by Prof. Jean Charamis who was unable to speak for some time due to the enthusiastic and prolonged applause he inspired; His Excellency, the Minister of Social Insurance; His Excellency, the Under Secretary of State; Frank Law, F.R.C.S.; Prof. E. S. Shivkov of Bulgaria; concluding with witty and cheerful remarks by Jules François which left us in a most joyful state of mind.

The Ladies Committee, under the leadership of Mrs. Charamis, had arranged a program of interest and pleasure for the ladies of the Congress consisting of daily visits to the various museums, temples, classical ruins, especially the Acropolis, Byzantine churches, monasteries, and so forth, for which Athens and its environs are noted.

These were the official functions. The Athenian ophthalmologists and their wives personally entertained various groups of delegates in their homes throughout the week. Their abundant kindness, hospitality, and graciousness, were overwhelming. It was all most enchanting.

The closing ceremony was quite informal and held before a dwindling, tired but happy audience. Appropriate remarks were made by Professor Charamis, by Professors Maggiore of Italy, Von Bahr (Sweden), R. Thiel (Germany), Vejdovsky (Czechoslovakia), Werner (Ireland) and concluded with an address by the highly efficient Secretary General, Professor Jules François. The few members remaining, then adjourned for a taking of the official photograph. Thus ended a most exciting and memorable occasion of great importance to world ophthalmology.

The newly elected officers of the society are Prof. G. von Bahr of Uppsala, Sweden, president; Prof. Jules François of Ghent, Belgium, secretary-general; and Prof. Adolphe Franceschetti of Geneva, Switzerland, treasurer. The next Congress will be held in May or June of 1964 in Vienna. At this meeting the official subject for discussion will be "The diagnosis and treatment of tumors of the eye and adnexa."

It is impossible to put into adequate words a description of this superb meeting. The stars of the performance were the hard working, hospitable, and affable men and women of the various local committees, led by their ever-charming and unruffled president, Jean Charamis assisted by his lovely wife, Angela, who won the hearts of everyone; and by Jules François, whose clever mind for conception and skilled hands for execution were everywhere present behind the scenes. This was a Congress that will be most difficult to equal and probably impossible to surpass.

Derrick Vail.

THE 19TH CLINICAL MEETING OF THE WILMER RESIDENTS ASSOCIATION

The Wilmer Residents Association is composed of former House Officers and Fellows of The Wilmer Ophthalmological Institute of The Johns Hopkins Hospital. The first clinical meeting was held on May 12, 13, and 14, 1938. The 19th meeting was held at The Johns Hopkins Hospital on April 7, 8, and 9, 1960. Approximately 435 ophthalmologists from the United States and Canada registered. Thirty-eight papers were read during the three-day session.

The program was opened on Thursday morning by A. E. Maumenee, director of the Wilmer Institute, who presented some cases of a "Congenital hereditary stationary corneal dystrophy." John M. McLean discussed "Urea as a therapeutic agent in ophthalmology." J. Lawton Smith listed the high incidence of "Ocular manifestations of the Pierre Robin syndrome." David Knox and Frank B. Walsh listed more pathologic changes from cranial injury in their paper "Head trauma: II."

Paul Chandler and A. E. Maumenee discussed detachment of the ciliary body as a "Major cause of hypotony and its treatment." Drainage of the subscleral fluid and diathermy with a penetrating electrode to close communication of the subscleral fluid with the anterior chamber has brought restoration of intraocular pressure and improvement of vision to some cases. Carteret Lawrence discussed the long-term results of peripheral iridectomy in the hands of the Wilmer resident staff in "Some aspects of closed-angle glaucoma." Lorenz E. Zimmerman showed the pathology of all stages of closed-angle glaucoma and pointed out the inflammation and necrosis of the optic nerve occurring in the acute case. Robert B. Welch and Henry E. Wahlen presented "Syndrome of peripheral retinitis, vitreous opacities and edema of the posterior pole," indicating the advantages of studying the pars plana in uveitis with retinal edema.

Charles W. Tillett and Grace M. Tillett presented two cases of "Corneal scarring due to contact lenses," and Norris L. Newton and Jack S. Gans presented "Some clinical uses of contact lenses." These papers stimulated so much general interest that a period was set aside for a general discussion of contact lenses and the responsibilities of the ophthalmologist.

J. Lane Reeves presented "Indications for therapeutic conjunctival flap," stressing the results obtained with very thin total flaps. J. Donald Gass reviewed the "Ocular manifestations of mucormycosis." John E. Eisenlohr, Arnall Patz, Paul A. Harper, Rowland V. Rider discussed "The relationship of myopia and prematurity." Angus L. MacLean discussed the surgical treatment of "Displacement of the lens." David Paton described "Conjunctival changes in sickle-cell disease" and demonstrated the high specificity and sensitivity of these changes as a clinical test for S-S and S-C disease. Robert I. Trent and Ernest A. Jones discussed the reading problem and presented interesting case histories showing improvement by the psychiatric and remedial reading approaches.

I. Willard Abrahams described the pathology of "Avian lymphomatosis and uveitis." Herman K. Goldberg and Maurice E. Langham discussed the use of Triethylene thiophosphoramide to prevent corneal vascularization. Maurice E. Langham showed "The measurement of aqueous humor formation in human eyes by the suction-cup technique." Later he gave a demonstration of this technique and fluorimetry in his laboratories.

Arnall Patz discussed "Experimental retinal arterial occlusion" and showed that high intraocular pressure protects the eye to some extent from the microscopically visible necrosis produced by vascular occlusion.

Louise Sloan gave "Some practical points on perimetry" and had an excellent demonstration of reading aids for the partially sighted. David B. Clark presented a case of "Aneurysm cutting optic tract." William Hoyt showed the "Vascular lesions of the visual cortex with hippocampal gyrus herniations." L. Harrell Pierce discussed his experience with the light coagulator in retinal detachment surgery, intraocular tumors, and inflammatory lesions.

William F. Knowles showed "The effect of intralamellar plastic discs on corneal physiology." Carl Kupfer and Ephraim Friedman discussed "Transcorneal potential in vivo." Leon Jacobs, Marjorie L. Melton, Ronald M. Wood, and Alan C. Woods discussed "Isolation of Toxoplasma from human uvea and retina." Robert A. Schimek and W. Lieberman showed the "Tonographic influence of Cyclogyl." William H. Zinkham presented "Enzyme studies on human lenses with primaquine sensitive erythrocytes." Arthur M. Silverstein and Sylvia Welter discussed further "Studies on experimental allergic uveitis."

Howard A. Naquin presented "Ablation of socket after enucleation" in older people who could not wear a prosthesis. J. Wallace McMeel discussed the "Use of Collistin in pseudomonas infection of the cornea." Robert Schimek showed his movie "Cataract ex-

traction by tumbling using alpha chymotrypsin, acetylcholine, 8-0 silk sutures."

William G. Marr presented "Pseudotumor cerebri syndrome after unilateral radical neck dissection." Richard Lindenberg presented "The pathology of circulatory disorders involving the lateral geniculate body." A. Harry Oleynick and David B. Clark presented "Corectopia with midbrain lesions." Richard Lindenberg conducted a "neuro-ophthalmology pathology conference," stressing the vascular supply to the visual cortex. The meetings were concluded with an excellent "neuro-ophthalmological clinic" conducted by Dr. Frank B. Walsh, including many interesting cases, for example, macular degeneration with a retinitis pigmentosalike fundus and pituitary involvement.

The 20th clinical meeting will be held March 23, 24, and 25, 1961.

Carteret Lawrence.

BOOK REVIEWS

Wolff's Diseases of the Eye. Revised by Richmond J. H. Smith, D.O., M.S., F.R.C.S. Springfield, Illinois, Charles C Thomas, 1959, fifth edition. 218 pages, 150 figures, 5 color plates, list of drugs, index. Price: $9.50.

The late Eugene Wolff, whose volumes on the *Anatomy of the Eye* and the *Pathology of the Eye* are widely known and used, produced the first edition of his book *Diseases of the Eye* in 1937. The fourth edition, the last under his hand, appeared in 1953. His successor in this venture is consultant ophthalmic surgeon, St. Mary's Hospital, among other appointments and is the Moorfields research fellow, The Institute of Ophthalmology, University of London. He has done the difficult job of revising and bringing up to date another man's popular book very well indeed.

It is a most attractive book, well printed on excellent paper and generously illustrated with sharp, clear plates. The original author's lucid style has been maintained, in spite of the fact that the chapter on glaucoma is completely rewritten, and others revised to include the advances in ophthalmology that have occurred in the last six years. Some out-of-date illustrations have been replaced by new and better ones. A useful and accurate list of drugs has been added.

This sound work is primarily designed for the student and general practitioner but the experienced ophthalmologist will find it useful for quick reference and teaching. The fact that five editions have appeared speaks well for the popularity that has been justly earned.

Derrick Vail.

You and Your Eyes. By Lawrence Lewison, O.D. New York, Trinity Publishing Corporation, 1960. 253 pages, 86 figures. Price: $3.50.

Caveat lector! The title is misleading and disguises a sales promotion venture for the Vent-Air Contact Lens, the exclusive property of Contact Lens Specialists. This outfit has branches in major cities from coast to coast and is undoubtedly one of the world's largest contact lens dispensers. Neither the book nor its jacket allude to this connection or mention that the author is employed by the Chicago office of this company. Instead, he is extolled as a pundit in the field of "sight without glasses" research. After a florid discussion of diet, visual exercises and the Bates method, aimed at those seeking to throw away their glasses, the master concludes that "most refractive difficulties rest on a firm basis of structural defect and so we must look to other means." The unwary reader now comes to the sales pitch. Hear ye! Hear ye! "The vented lens came to dominate the contact lens picture. . . . The vexatious problem of application and removal became a matter of great simplicity. . . . Extended wearing time with full comfort—in some cases weeks and months without removal was

not a rarity. . . . With the vented lens in single vision, double vision and triple vision forms, all the benefits of contact lenses could now be offered, almost irrespective of the refractive correction. . . . The effect of the lens apparently reduced the myopia in many cases, and in other myopic cases it retarded its progression. . . . Newspaper stories described the transformation in the partially-sighted through the miracle of a contact lens-telescopic system. Restoration to ordinary pursuits—even obtaining a driver's license, has been the good fortune of many. . . . More than six million persons in need of visual correction are gaining it through these invisible aids."

A personal case report of his is astounding! "A 23 year old girl had been wearing very thick glasses prescribed for congenital cataract since the age of 8. With her glasses visual acuity was not better than 20/100. Contact lenses were advised. Her vision improved to 20/25. Within two weeks she was wearing a new outfit, her hair was done smartly, and cosmetics were used for the first time. This points up the triggering effect invisible vision correction has in upgrading appearance and personality."

This book, with its melange of truths, half-truths and non-truths, is a revelation of what the contact lens situation is and a premonition of what may come.

James E. Lebensohn.

LES SYNDROMES OCULO-CUTANES. By Pierre Lèbas. Number 124, Fasicule 1, of the Bulletin de la Société Belge d'Ophtalmologie, Brussels, Imprimerie Medicale et Scientifique, 1959. 833 pages, 81 illustrations, references. Price: Not listed.

Although this is not published as a book by itself, but is part one of the four numbers of the Belgian Society's *Bulletin* brought out each year, it deserves the attention and spotlight of a special review. I know of no comparable volume in English. This is a pity, for the subject is one of great importance to the clinician and the large number and widely scattered papers in the literature have deserved, ere this, to be brought together under one cover. The 20 chapters contain complete reviews of phakomatosis, skin diseases associated with cataracts, collagen diseases, sarcoidosis, pemphigus, bullous dermatoses, Béhçet's disease, Reiter's syndrome, diseases of elastic tissue (for example, angioid streaks), Vogt-Koyanagi-Harada's disease, congenital ectodermic dysplasias, pigmentary disturbances, lipoidosis, ichthyosis, acne rosacea, xeroderma pigmentosum, molluscum, contagiosum, diverse dermatoses, general diseases with skin and ocular manifestations, and avitaminosis.

The book is well written and illustrated. The author has been skillful in extracting and putting together in textbook fashion the widely scattered information in the world literature of the subject. I wish very much that it could be translated and published in English.

Derrick Vail.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Conrads, Hans. **Regenerative changes in the corneal innervation.** Ophthalmologica **138**:365-369, Nov., 1959.

The cornea of rabbits was cauterized with silver nitrate; 14 days later a process of regeneration of the injured cells was demonstrable. In the center of a complex mass of reactive lymphocytic and leucocytic cells a "nervous" fibrillar network was seen to have developed. In the periphery of this site one saw spicular cells developing from stromal cells. The joining of peripheral and central fibrillar networks gave rise to a new nerve supply for the cornea. (4 figures, 9 references)

F. H. Haessler.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Ashton, N. and Choyce, D. P. **Pathological examination of a human eye containing an anterior chamber acrylic implant.** Brit. J. Ophth. **43**:577-583, Oct., 1959.

Macroscopically the lens appeared to fit closely into the chamber angle. There was no contact with the corneal epithelium. Microscopically the iris was pushed backward, and was adherent to the ciliary body. The tissue of the corneo-iridic angle was compressed to form cups of atrophic tissue, extending into the ciliary body. On both sides the ciliary muscle was stretched, atrophic and torn away from the scleral spur. No eosinophiles or giant cells were formed. There was considerable edema of the macula. There was no evidence of sympathetic or foreign body reaction. (6 figures, 20 references)

Irwin E. Gaynon.

Frandsen, E. **Eye disease following BCG Vaccination. Studies of the significance of tuberculosis in the etiology of certain eye diseases, with particular reference to ocular complications after BCG vaccination.** Acta ophth. Suppl. 57, 1959.

The author's summary of this 170-page monograph occupies five and one-half pages, and it is impossible to summarize the summary without making the contents meaningless. The material consists of 1,158 patients with conditions commonly associated with tuberculosis. In 72 of them the eye disease had appeared after

BCG vaccination. It is concluded that BCG vaccination may undoubtedly be the cause for phlyctenular keratoconjunctivitis; it can, in rare cases, give rise to iridocyclitis and choroiditis, and certain case histories suggest that periphlebitis may also be caused by it. (40 tables, 4 figures, 321 references). John J. Stern.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Menna, F. and Lamberti, O. **The action of chymotrypsin on the reabsorption of experimental hyphema.** Arch. di ottal. **63**: 397-406, Sept.-Oct., 1959.

The authors discussed the properties of proteolytic enzymes at length. Chymotrypsin was shown to dissolve clots of blood, possibly by altering prothrombin. The presence or lack of calcium had no apparent effect. Chymotrypsin appeared also to be an anticoagulant.

For the experiment guinea-pig blood was injected to completely fill one anterior chamber. Then half the animals were treated by intravenous injection of 2.5 mg. of chymotrypsin twice daily. The reabsorption time in the treated animals was half that in the controls. (1 figure, 23 references) Paul W. Miles.

Suvanto, E., Reissell, P. and Himanka, E. **Retinal circulation time in man.** Acta ophth. **38**:46-49, 1960.

A method is described in which dye is injected into the internal or common carotid artery. The average time lapse between appearance of the dye in a retinal artery at the optic disc and its appearance in a vein at the same place is 1.3 seconds. (1 table, 4 references) John J. Stern.

Wistrand, Per. **The effect of carbonic anhydrase inhibitor on intra-ocular pressure with observations on the pharmacology of acetazolamine in the rabbit.** Acta Pharm. & Toxicol. **16**:171-193, 1959.

After administering the carbonic anhydrase inhibitor acetazolamine to rabbits, values for plasma concentration and half life, plasma-protein binding, concentration in erythrocytes, urinary excretion and penetration into ciliary processes, lens, cornea, vitreous body and anterior and posterior aqueous humors were obtained. The results were correlated with the response of intraocular pressure to different routes of administration, single or repeated intravenous injections, and continuous infusions.

The effect on intraocular pressure was directly related to the concentrations in the plasma and ciliary processes, tissues from which the drug disappeared at about the same rate. The effect was not related to the amount of "bound" drug in the red cells. (7 figures, 4 tables, 50 references) Author's summary.

Wynands, J. E. and Crowell, D. E. **Intraocular tension in association with succinylcholine and endotracheal intubation; a preliminary report.** Canad. Anaesth. Soc. J. **7**:39-43, Jan., 1960.

It seems unlikely that succinylcholine should not be used for intubation; the rise of ocular pressure will have been dissipated long before the surgeon is ready to open the eye. However, a single large dose of this drug should not be administered when the eye is open for intraocular surgery. F. H. Haessler.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

François, J. and Verriest, G. **Three new observations of atypical congenital achromatopsia.** Ann. d'ocul. **193**:123-137, Feb., 1960.

The authors continue their study of congenital achromatopsia and report three cases of atypical color weakness. All show reduced visual acuity. However, cases 1 and 2 (in cousins) show a photopic lumi-

nosity curve of the scotopic type while the third case shows a protanopic type. (5 figures, 3 tables, 7 references)

David Shoch.

Mercier, Armand. **Evolution of ophthalmologic problems posed by the progress in aviation.** Ann. d'ocul. **193**:138-160, Feb., 1960.

The author reviews the effect of stratospheric and supersonic flight on visual function. He discusses these effects under four headings: velocity, acceleration, vibration and altitude. All these entities of themselves are capable of diminishing visual performance and they must be controlled where possible. In addition, pilots must be checked frequently so that any ill-effects may be found at the earliest possible moment. (2 figures, 45 references)

David Shoch.

Oppel, O. **Current concepts about the nature of functional amblyopia.** Klin. Monatsbl. f. Augenh. **136**:1-20, 1960.

Active cortical inhibition (Tschermak) is believed to be the cause of certain deficiencies of the amblyopic eye. Such defects are: decrease of central vision, decrease of the pupillo-motor quotient (Harms), retinal rivalry in favour of the sound eye, gnostic disturbances, "crowding," eccentric fixation, and difficulties in localization. The author was also able to demonstrate a slight anomaly of the cone behavior during dark adaptation in amblyopic eyes.

The active inhibitory centrifugal impulses are believed to extend from their point of origin in the occipital cortex to the retinal elements as well. These impulses may lead to partial or complete interruption of the "optognostic" apparatus, that is, cone vision. The latter is phylogenetically the highest visual function and is dependent on continuity of a 1:1 retinocortical relationship. The author implies that all the characteristic features of the amblyopic eye can be explained by inhibitory influences upon the optognostic apparatus. (8 figures, 7 tables, 5 references)

Gunter K. von Noorden.

Zagora, Edward. **Observations on compensatory adjustments in one-eyed persons.** Brit. J. Ophth. **43**:596-601, Oct., 1959.

Uniocular torticollis is demonstrated in a one-eyed person by tilting of the head toward the shoulder of the sound eye, turning the face to the side of the lost eye, and depression of the chin toward the chest. This is done in an attempt to enlarge the nasal field. In the correction of refractive errors care must be taken that the bridge, frame and temples do not restrict the nasal field. (4 figures, 1 table, 2 references)

Irwin E. Gaynon.

5

DIAGNOSIS AND THERAPY

Arasimowicz, C. and Chwirot, R. **Surgical access to the optic nerve in the dog.** Ophthalmologica **138**:381-388, Nov., 1959.

The authors describe a simple surgical procedure which provides adequate access to the optic nerve with a minimum of trauma. (4 figures, 12 references)

F. H. Haessler.

Bertelsen, T. I. **A new and improved technique in orbital pneumography.** Acta ophth. **38**:57-61, 1960.

After topical anesthesia, a 3 mm. incision is made through conjunctiva and Tenon's capsule at 2 o'clock, 6 to 7 mm. from the limbus. A purse string suture is inserted and a blunt tear duct cannula introduced 1 cm. and directed below the posterior pole. After tightening the suture, 4 to 6 cc. of air are insufflated slowly, the cannula removed, and the suture closed tightly. This method is safer and more effective than others and allows X-ray visualization of the orbit and its soft tissue contents. It may be necessary

to introduce air retrobulbarly as well; 15 cc. are injected with the same technique as is used for retrobulbar anesthesia. (2 figures, 3 references) John J. Stern.

Claythorne, N. W. B., Rottenstein, H. S. and Dripps, R. D. **Effect of succinylcholine on intraocular pressure in adults, infants and children during general anesthesia.** Anesthesiology **21**:59-63, Jan.-Feb., 1960.

Succinylcholine caused a rise in tension in one half of 54 patients and it disappeared promptly after cessation of the drug action. The rise was unrelated to the anesthetic agent or pupil size and the tension was moderately reduced with deeper anesthesia. No harm to vision was noted and it is unlikely that any harm will arise from use of this drop except during surgery for cataract. F. H. Haessler.

Krannig, H. D. **Diagnosis of vitreous hemorrhages in eyes with opaque anterior chambers.** Klin. Monatsbl. f. Augenh. **135**: 839-842, 1959.

Transscleral illumination and observation of the opposite illuminated aspect of the sclera will reveal the presence of localized or diffuse vitreous hemorrhage. This method is of diagnostic and prognostic value in eyes where direct observation of the vitreous is prevented by extensive hyphema. (3 figures, 8 references)

G. K. von Noorden.

Mikuni, M. and Yoneyama, T. **A new ophthalmodynamometer.** Klin. Monatsbl. f. Augenh. **136**:21-34, 1960.

Bailliart's instrument is still the most widely used by ophthalmologists. This method, however, has several disadvantages. Kukan developed a different approach to ophthalmodynamometry. A suction cup is applied to the ocular wall. If suction is employed positive pressure acts on the eye in an area corresponding to the margin of the cup. This increases the intraocular pressure. The authors have improved Kukan's instrument. Suction cups of different sizes are available and can be connected with a vacuum pump and a sphygmomanometer. By measurements on 200 living eyes the suction cups were calibrated. The authors believe that this method of applying pressure to the eye during dynamometry is far superior to that with other instruments in use. (8 figures, 7 tables, 5 references)

Gunter K. von Noorden.

Oksala, A. **The echogram in detachment of the retina.** Ophthalmologica **138**: 350-361, Nov., 1959.

The author has devised a method for using the echogram in the diagnosis of retinal detachment. It makes the location of the detachment and the subretinal space recognizable and makes it possible to recognize the presence of tumor with certainty. This is true even when the detachment is no greater than 1.7 or 1.8 mm. and when it is not recognizable ophthalmoscopically because of cataract or vitreous opacity. (8 figures, 6 references)

F. H. Haessler.

Oksala, A. and Lehtinen, A. **Use of the echogram in the location and diagnosis of intra-ocular foreign bodies.** Brit. J. Ophth. **43**:744-752, Dec., 1959.

Foreign bodies such as slivers, stones, wood chips, and glass cannot be easily seen on X-ray film. An ultrasound echogram is an aid in locating the site and the size of the intraocular foreign body. The larger the foreign body the longer is the echo.

The apparatus and technique are described. With the aid of plexiglass the echogram will record as close as one millimeter to the surface of the cornea. The ultrasonic diagnosis is as accurate as X-ray exploration in the anterior surface of the eye. For the deeper sites the use of X-ray is the method of choice. (11 figures, 5 references) Irwin E. Gaynon.

Öksala, A. and Lehtinen, A. **Magnification of the echogram of the eye by a high-frequency oscilloscope.** Acta ophth. **38**:19-24, 1960.

By connecting the ultrasonic apparatus to a Tektronix oscilloscope type 545, the acoustic magnification can be increased to 340 times compared to a magnification four times with conventional equipment. (5 figures, 12 references) John J. Stern

Öksala, A. **Analysis of echoes from the posterior bulbar wall.** Acta ophth. **38**:25-31, 1960.

The thickness of the sclera and of retina plus choroid, can be measured by the echogram. In the latter instance, one of the membranes has to be about four times and both together about three times as thick as normal. This method can be useful in the diagnosis of posterior scleritis, rupture of the sclera, and some other conditions. (7 figures, 12 references)

John J. Stern.

Sachsenweger, R. **Evaluation of disability in visual field loss combined with reduction of visual acuity.** Klin. Monatsbl. f. Augenh. **136**:102-106, 1960.

The author suggests that the evaluation of disability in a combination of the two conditions mentioned in the title be carried out by means of diagrammatic tables. (2 figures, 2 tables)

Gunter K. von Noorden.

Sedan, Jean. **Efficacy of convex cylinders for near vision in migrainous myopic astigmats of small degree.** Ann. d'ocul. **193**:245-248, March, 1960.

The authors state that they have been able to cure many cases of migraine in myopic patients with astigmatism of small degree by prescribing plus cylinders. Seven cases are tabulated in which the correction is changed from a small minus cylinder axis 180 to a small plus cylinder axis 90. The resultant minus sphere that results from the transposition is dropped so that actually the effect is that of using an addition for near. All patients were apparently cured. (1 table)

David Shoch.

Zuckerman, Joshua. **Impaired or absent fundus reflex (with special reference to obstruction by cataract).** Arch. Pediat. **77**:14-27, Jan., 1960.

The author points out to the pediatrician that, having excluded other possible causes of opacity of the lens, he must search for detachment of the retina. Early operation is important so that retinal function will develop normally. (12 figures) F. H. Haessler.

6

OCULAR MOTILITY

Venco, L. and Valvo, G. **Clinical statistical considerations of concomitant convergent strabismus and of divergent strabismus. Part I and Part II.** Arch. di ottal. **63**:407-436, Sept.-Oct., 1959.

This is an excellent review of a large number of cases seen at l'Ospedale Civile di Brescia. The authors list the exact routine used in motility cases, including atropine refraction, Cupper's method for amblyopia ex anopsia, orthoptics in errors of 10 to 15 degrees, and surgery.

The authors operated upon 342 patients; most commonly the operation was bilateral recession but many had an additional resection. The medial rectus muscles were recessed from three to eight mm. Many surgeons are unwilling to exceed a conservative four mm. for fear of impaired convergence. Usually the amount of bilateral recession was in proportion to the strabismus, about three mm. for 10 degrees, and eight mm. for 35 degrees. In the resections, the authors expected an additional five degrees from an eight-mm. resection or advancement. The maximum resection-advancement re-

ported was 15 mm. Children required less surgery per degree of esotropia.

Of the 342 patients operated upon, 307 were corrected to within six degrees of esophoria and three of exophoria by one procedure, 25 were undercorrected, and 10 were overcorrected. Five patients were operated upon for a second time, and one for a third.

Of 57 patients with exotropia 49 were treated surgically. For eight degrees of error, one lateral rectus muscle was recessed. For 15 to 18 degrees, both lateral rectus muscles were recessed. For 25 degrees or more, resection of the internal rectus muscle was added. One can obtain additional five degrees from a six-mm. resection or advancement. A resection of 12 mm. produces a 20 degree effect.

For intermittent divergence excess the authors advise a recession of one lateral rectus muscle. For convergence insufficiency they advised advancement of one internal rectus muscle. (1 table, 28 references, Part I. 25 references, Part II)

Paul W. Miles.

7

CONJUNCTIVA, CORNEA, SCLERA

De Rosa, C. **A case of keratoconus posterior.** Arch. di ottal. **63**:445-455, Sept.-Oct., 1959.

A ten-year-old child was found to have bilateral congenital corneal opacities, 9 diopters of myopia, and corrected vision of 3/10. Upon examination only the central five-mm. portion of each cornea appeared involved. The epithelial surface appeared normal and of normal curvature (7.5 × 7.4 mm. radius). The central portion of the cornea was thin, and the endothelial surface shaped like a gothic arch. The opacities were parenchymal. The anterior chamber, iris and lens were normal. The fundus showed myopic changes in each eye.

The cause of the disturbance was possibly an intrauterine inflammatory necrotizing keratitis. (2 figures, 21 references)

Paul W. Miles.

Forsius, H. **The refractive power of the cornea and embryontoxon corneae posterius in high degrees of hypermetropia.** Acta ophth. **38**:5-15, 1960.

Of 122 cases of hypermetropia of 5 D or more (7 D or more in 54), this vision of 0.8 or better was noted in 39 percent; the average was 0.59. The refractive power of the cornea was significantly lower (42.4 against 43.50 D in 315 control cases). Of 116 eyes 29 had posterior embryontoxon (14 out of 114 in the controls) and 29 out of 109 eyes had hypoplasia of the iris or persistent pupillary membrane (9 out of 114 controls). One patient had glaucoma simplex and three had closed-angle glaucoma, and 26 of 56 patients had strabismus (46 percent in hypermetropia below 7 D, 48 percent in hypermetropia above 7 D). In 14 out of 102 cases pseudopapillitis was observed whereas this was found in only six of 114 controls. In nine cases there was a difference of 2.5 to 7.25 diopters in the right and the left eye. (8 tables, 17 references) John J. Stern.

Gilkes, M. J. **Snake venom conjunctivitis.** Brit. J. Ophth. **43**:638-639, Oct., 1959.

A case of snake venom conjunctivitis is presented. The conjunctival vessels were prominent and nummular "mutton-fat" deposits were seen on the posterior surface of the cornea. The eye was irrigated and penicillin-streptomycin ointment was instilled. The next day the eye was almost healed. (1 reference)

Irwin E. Gaynon.

Hoffmann, D. H. **Bilateral episcleritis with panchondritis.** Klin. Monatsbl. f. Augenh. **135**:844-846, 1959.

Panchondritis belongs to the group of collagen diseases. The later stages of this

rare condition are characterized by a generalized chondromalacia. Episcleritis was observed in both eyes of a 34-year-old patient with panchondritis. Systemic steroid therapy as well as prednisolone drops used topically influenced the course of the disease favourably. (2 figures, 9 references) G. K. von Noorden.

Jordana Barea, Jose. **A contribution to the prophylaxis of trachoma.** Arch. Soc. oftal. hispano-am. **19**:900-905, Nov., 1959.

The interesting feature of this contribution emerges from the graph, plotting the time of onset of the infection. It shows that familial infections usually take place in the first years of life, while extrafamilial contamination occurs mostly in adolescents and adults. (1 graph, 8 references) Ray K. Daily.

Mathur, S. P. and Mathur, B. P. **Conjunctival amyloidosis.** Brit. J. Ophth. **43**: 765-766, Dec., 1959.

Primary amyloidosis of the conjunctiva leads to tumor formation of the tarsal plate. In the cases reported it is likely that primary amyloidosis bears some relation to trachoma. The trachoma virus inhabits the tarsus in the chronic stage. Cases of hypertrophy of the tarsal plate and conjunctiva should be examined microscopically for amyloidosis. (8 references) Irwin E. Gaynon.

Mathur, S. P. **Two cases of conjunctival cyst.** Brit. J. Ophth. **43**:763-764, Dec., 1959.

Two cases of conjunctival cyst associated with an overlying pterygium are described. A congenital origin is suggested because of the freedom from superficial pterygium and its attachment to the deeper structures. (5 references) Irwin E. Gaynon.

Mestre Espinach, Juan. **Histopathologic characteristics of keratoconus.** Arch. Soc. oftal. hispano-am. **19**:908-913, Nov., 1959.

The material of this study comprises eight cases of keratoconus operated by Joaquin Barraquer. Applying Amsler's classification one of these cases is in grade two, two are in grade three, and five in grade four. The histopathologic findings are correlated to the clinical classification of the disease. The conclusions emerging from this study indicate that the disease begins in Bowman's membrane, advances anteriorly, and finally involves the epithelium. The weakened cornea begins to distend and the irritative phenomena produce a proliferation of connective tissue, the resistance of which checks the progress of the ectasia. The changes in the posterior portion of the cornea are the consequences of the changes in the anterior layers. Ray K. Daily.

Norn, M. S. **Cytology of the conjunctival fluid. Experimental and clinical studies based on a quantitative pipette method. M.D. Thesis.** Acta ophth. 1960, suppl. 59.

In this 152-page monograph, which is the thesis presented by the author for the doctorate, he provides a brief historical review of the subject before he gives a survey of the composition of the conjunctival fluid and of the origin of its individual components. After reviewing the methods used for cytologic examination of the conjunctiva the author describes his pipette method, which is approximately quantitative, and allows sampling from a single layer, the aqueous phase of the conjunctival fluid. The pipette is provided with a rubber bulb, by means of which conjunctival fluid is sucked from the lateral area of the inferior fornix or inferior tarsus. The bulb is removed and the fluid in the pipette is diluted with a fixative (10 percent formalin). Then the total amount of fluid is pressed out on to a slide, where it is allowed to dry up before staining. Formolfuchsineosin as well as

Eskelund's staining were the methods preferred for the pipette specimens.

The different layers of the conjunctival fluid and the conjunctiva are described, and these are compared with the various components of scrapings and pipette specimens.

The composition of the conjunctival fluid varies from area to area in the conjunctiva. The greatest numbers of cells are found laterally in the inferior fornix and inferior tarsus. The number of neutrophils often rises in the course of the night, possibly because of the presence of bacteria, to fall abruptly immediately on awakening.

Strong eye drops, such as silver nitrate, cause considerable epithelial desquamation, which is followed by a pronounced rise in the number of neutrophils. Weaker irritants bring about a similar, though less pronounced change of the conjunctival cytology, while a few substances which cause very little or no irritation seem not to alter the cytologic picture. Vasoconstrictors reduce the numbers of all cell types.

A rise in the number of neutrophils in the conjunctiva can be provoked by a reflex action (from the contralateral conjunctiva or the nasal mucosa).

The conjunctival epithelium scales off after death. In later chapters the individual cytologic phenomena observed are described. Neutrophilia (i.e. 100 or more neutrophils in the pipette specimen, and the number of neutrophils exceeding that of lymphocytes) is always present in cases of infectious, bacterial conjunctivitis, but never in normals. Eosinophilic leukocytes occur solely in allergic conjunctivitis, often in a small number only. The number of lymphocytes varies. Lymphocytosis is frequently seen in the normal conjunctiva, and always in viral and follicular conjunctivitis, unless there is neutrophilia. Increased epithelial desquamation is most often found in association with neutrophilia.

An increased number of nucleated squamous cells is also seen in cases where a conversion occurs into squamous epithelium.

The bacteriologic and the cytologic findings are compared. Mention is made of chemoresistance tests, occurrence of fungi, and histologic examination of biopsy specimens are compared with simultaneous cytologic analyses.

F. H. Haessler.

Pierse, D. and Casey, T. A. **Lamellar keratoplasty.** Brit. J. Ophth. **43**:733-743, Dec., 1959.

A series of 48 lamellar corneal grafts are reported. One third of these were done as an out-patient procedure. Prior to surgery the intraocular pressure is reduced by retrobulbar injection of hyaluronidase plus xylocaine and pressure on the globe. A combined overlay and direct suture is used. A needle guide for corneal suture and a holder for the graft, much like the erisophake of Bell, is described. A rectangular graft is used. The donor cornea is removed in toto and the lamellar separation is made by a tearing rather than a slicing technique. Nine cases of malignant pterygia were treated with a graft that extended two millimeter onto the sclera. Four cases of active herpetic keratitis of more than two months duration showed prompt improvement. Thirteen cases of recurrent keratitis (herpetic, mustard gas and acne rosacea) had no postoperative recurrence. With marked corneal vascularization a smaller penetrating graft has a much better chance of success. (4 figures, 4 references)

Irwin E. Gaynon.

Wilczek, M. **Plastic repair of the conjunctiva.** Klin. Monatsbl. f. Augenh. **135**:822-827, 1959.

Excess conjunctiva from the upper fornix is utilized to cover large defects of the bulbar conjunctiva. Cosmetic and functional results are excellent in patients operated upon by the author's method. (12 figures, 6 references)

G. K. von Noorden.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

De Rosa, C. **Two familial cases of heterochromic cyclitis of Fuchs complicated by glaucoma.** Arch. di ottal. 63:437-444, Sept.-Oct., 1959.

Of cases of heterochromic cyclitis reported in the past, 13 percent were said to be bilateral, 14 percent developed glaucoma, and 25 percent were associated with pigmentary anomalies of the skin. Many appeared not to be familial. Those reported here were in siblings with no other family history. The glaucoma first appeared at age 62 and 64 years, and in each case it appeared in the eye which was not aphakic from removal of a cataract. The aphakic eye in each case escaped disease. In each case, the abnormal eye was relatively hypochromic with iris atrophy, redness, blur, corneal edema, keratic precipitates, flare, and tension about 50. Both were treated surgically by sclerectomy and iridectomy, but results were not good from a visual standpoint. (1 figure, 18 references)

Paul W. Miles.

Etienne, R. **Essential atrophy of the epithelial layers of the iris and ciliary body; its relationship to glaucoma.** Ann. d'ocul. 193:97-122, Feb., 1960.

The syndrome of "pigmentary glaucoma" is related to essential atrophy of the epithelium of the iris and ciliary body (this is not "essential iris atrophy"). The clinical characteristics of this syndrome are: a Krukenberg spindle; pigmentation of the trabeculum, the anterior face of the iris, the equator of the lens and the zonular fibers; atrophy of the epithelial layers of the iris; a Tyndall effect in the anterior chamber; and finally glaucoma. Twelve cases of this syndrome are presented in nine of which there was an associated glaucoma. (The second part of this article will appear next month.) (3 figures, 1 table)

David Shoch.

Etienne, R. **Essential atrophy of the epithelial layers of the iris and ciliary body; its relationship to glaucoma. Part II.** Ann. d'ocul. 193:224-244, March, 1960.

This is the conclusion of a two-part article, part one of which appeared in the February, 1960, issue. The author feels that the deposition of pigment on the trabeculum in this syndrome is responsible for the glaucoma. He cites a case of bilateral atrophy of the epithelium of the iris where pigment was deposited only in one angle. This eye developed glaucoma whereas the eye without pigment in the angle did not.

A comparison is made of this entity and pseudo-exfoliation of the capsule in tabular form. The author concludes that these may be two forms of a basic underlying disease of the epithelial layers of the iris and ciliary body. He also suggests that such entities as Fuchs' heterochromia iridis may be in the same family of diseases. All these glaucomas are basically uveal in origin and should be classified as secondary glaucoma. However, the appearance of unusual vessels and pigment in the angle in some of these cases also justifies a classification of congenital glaucoma.

The author emphasizes that one of the most valuable clinical tests is transillumination which demarcates the epithelial atrophy of the iris better than direct examination. (1 figure, 2 tables, 51 references)

David Shoch.

Fuchs, A. **Proliferating choroiditis. A chapter from "Geography of Ophthalmic Diseases."** Klin. Monatsbl. f. Augenh. **135**:775-791, 1959.

Six cases were observed by the author in the Far East. Characteristic changes were present, such as bands of connective tissue under the retinal vessels and large white areas which covered the choroid. Choroiditis proliferans is thought to occur after replacement of a formerly detached retina. The detachment may have been idiopathic, secondary to Harada's disease, Hippel's disease, or to circinate retinopathy. (17 figures, 13 references)

G. K. von Noorden.

Haarr, M. **Rheumatic iridocyclitis.** Acta ophth. **38**:37-45, 1960.

Among 527 patients with acute and chronic iridocyclitis, X-ray changes compatible with Bechterew's disease were found in 40.9 percent of the men and 17.3 percent of the women with acute iridocyclitis. Chronic polyarthritis was found in 1.6 percent of men and 2.5 percent of the women with acute iridocyclitis and 3.7 percent and 3.4 percent respectively of those with chronic iridocyclitis. Out of 153 patients with Bechterew's disease (119 male and 34 female), and 97 with chronic polyarthritis (49 male and 48 female), 32.6 percent of those with Bechterew's disease had one or more attacks of iridocyclitis, against 4.1 percent of those with chronic polyarthritis. These findings indicate that these two conditions are different. Urogenital infection may be the cause for the preponderance of men with acute iridocyclitis and therefore a causative factor in Bechterew's disease. (5 tables, 16 references) John J. Stern.

9

GLAUCOMA AND OCULAR TENSION

van Beuningen, E. G. A. **Pigmentary glaucoma and the significance of chamber-angle pigmentation for the development of glaucoma.** Klin. Monatsbl. f. Augenh. **135**:796-802, 1959.

The question whether or not pigmentary deposits on the trabecular meshwork cause glaucoma, or vice versa, remains a matter of discussion. Two cases of juvenile pigmentary glaucoma and one of senile pigmentary glaucoma are reported. All three patients responded well to a trephine procedure. Pigmentation of the chamber angle is not always associated with glaucoma. It may be secondary to chronic simple glaucoma, contusion of the globe, and diabetes. In pigmentary glaucoma other factors than pigmentation of the filtering structures must play a significant etiologic role. (3 figures, 8 references) G. K. von Noorden.

Coop, D. H. **Neptazane in glaucoma. A preliminary clinical report.** Brit. J. Ophth. **43**:602-612, Oct., 1959.

Neptazane is a carbonic anhydrase inhibitor and it resembles diamox chemically. Neptazane is excreted more slowly, penetrates the aqueous more readily, and maintains a higher concentration in the blood plasma than diamox. Doses of 125 to 250 mg. of Neptazane were used once daily. There was a latent period of three to five hours. The fall in tension lasted about 16 to 18 hours. In some instances the fall in tension from a single dose of Neptazane lasted several days. Proper spacing of the drug was difficult at times. With repeated doses the drug began to lose its effect.

The side effects of Neptazane tend to be less than those of diamox because of the much smaller dosage used. These consisted of anorexia, nausea, vomiting, shortness of breath, palpitation and paresthesia. The response to a single dose in simple glaucoma was good. In acute narrow-angle glaucoma diamox, given intravenously, is still the drug of choice. (12 figures, 2 references, 14 case reports)

Irwin E. Gaynon.

Draeger, J. and Käfer, I. **A contribution to the history of tonometry. The first impression tonometer (A. von Graefe, 1862).** Klin. Monatsbl. f. Augenh. **135**:846-852, 1959.

Early efforts to determine ocular tension quantitatively are discussed. The first tonometers (von Graefe, 1862, and Donders, 1863) are described and illustrated. (4 figures, 7 references)

G. K. von Noorden.

Foulds, Wallace S. **Observations on the facility of aqueous outflow in closed-angle glaucoma.** Brit. J. Ophth. **43**:613-621, Oct., 1959.

In closed-angle glaucoma the dark room test may result in a rise in ocular tension and a fall in the facility of aqueous outflow. Of the 97 glaucomatous eyes tested, 67 percent gave a change in outflow, the mean reduction being 50 percent of the initial figure, while in 30 percent a rise in ocular tension of more than 8 mm. Hg was noted. Time is required for a rise in ocular tension after closure of the chamber angle.

The angle may be closed by goniosynechiae or by reversible irido-corneal contact and consequently gonioscopy is less helpful than might be expected. A definite correlation is found between the prevailing level of aqueous outflow and that of the ocular tension. In 83.3 percent of the tests the results were positive when the facility of outflow was less than 0.12, whereas this was true in only 17.7 percent of the tests when it was greater than 0.13. The lower the initial outflow level, the higher the rise in ocular tension. When the angle is largely obstructed prior to the test the remaining open sector is more sensitive to change in illumination. (6 figures, 8 references) Irwin E. Gaynon.

Haye, C. **The syndrome of Posner-Schlossmann.** Ann. d'ocul. **193**:161-164, Feb., 1960.

The characteristics of this syndrome are an acutely elevated tension without pain or redness, minute pale cells on the corneal endothelium, but no true flare, no synechiae, and a minimal amount of discomfort. Response to miotics and cycloplegics is poor. Response to steroids and diamox is good. No evidence of glaucoma is present between attacks. (4 references)

David Shoch.

Jensen, V. J. **Acute glaucoma following carotid arteriography.** Acta ophth. **38**:32-36, 1960.

A case of this syndrome is described and the histopathologic findings are discussed. (1 figure, 9 references)

John J. Stern.

Langham, Maurice E. **Influence of the intra-ocular pressure on the formation of the aqueous humour and the outflow resistance in the living eye.** Brit. J. Ophth. **43**:705-732, Dec., 1959.

Compensatory reactions take place when the intraocular pressure is increased by infusion. The reactions are dependent upon an intact sympathetic supply to the eye. The injection of acetazoleamide inhibits the secretion of aqueous humor without affecting the general blood supply. Unilateral ligation of the common carotid artery has little effect on intraocular dynamics.

Aqueous humor formation, outflow resistance and episcleral venous pressure did not remain constant with increased intraocular pressure. As the intraocular pressure increased there was a decrease in either the aqueous humor formation or in the outflow resistance.

This study, by the use of intravenous injection of acetazoleamide, unilateral ligation of the common carotid artery, section of the preganglionic cervical sympathetic fibers, and intraocular injections of the enzyme hyaluronidase, shows that tonography does not measure resistance

in the untouched eye. (14 figures, 44 references) Irwin E. Gaynon.

Leydhecker, W. **The choice of surgery in primary glaucoma of the adult.** Klin. Monatsbl. f. Augenh. **135**:802-811, 1959.

Surgery in primary chronic glaucoma is indicated when field loss occurs, the tension increases in spite of miotics, and life expectancy is more than ten years. In older patients surgery is procrastinated, in the younger age group one is more apt to operate sooner. Surgery is indicated in acute glaucoma when the attack has not subsided under medical treatment after six to 12 hours. The procedures in iridencleisis, trepanation, iridectomy ab externo, and cyclodiathermy are discussed, and the therapeutic effect of each is evaluated on the basis of figures from the literature. Iridectomy is the procedure of choice in primary acute congestive glaucoma, but it cannot be recommended in the presence of extensive synechia and poor outflow facilities. Cyclodialysis is used in aphakic glaucoma and should never be carried out in eyes with an extremely narrow angle. Cyclodiathermy rarely reduces the pressure to less than 20 mm. Hg and the therapeutic effect of this procedure is of short duration. Cyclodiathermy is used, however, as a second procedure after unsuccessful fistulization or where intraocular surgery seems inadvisable.

G. K. von Noorden.

Stepanik, J. **The influence of chlorothiazide on the ocular tension in man.** Ophthalmologica **138**:361-364, Nov., 1959.

In 36 patients diamox produced a statistically highly significant decrease in tension whereas the tension remained unchanged under the influence of chlorothiazide. Treatment with chlorothiazide decreased the pressure-lowering effect of diamox. (1 figure, 6 references)

F. H. Haessler.

Valu, L. and Csüllög, F. **Our experiences with problems and results in surgery of glaucoma simplex.** Klin. Monatsbl. f. Augenh. **135**:811-819, 1959.

Eyes with glaucoma simplex should not be operated upon until a full evaluation of all visual functions has been made. The first impression of the examiner may often be misleading. It has been observed that visual functions do not necessarily decrease in the presence of longstanding elevated pressure. If surgery is inevitable the authors prefer a cyclodiathermy when the tension is less than 40 mm. Hg, and a peripheral iridectomy with tensions over 40 mm. Hg. (2 figures, 6 tables, 12 references) G. K. von Noorden.

10
CRYSTALLINE LENS

Binkhorst, C. D. **Indication and implantation technique of the "pupillary lens" or the "iris clip lens" in aphakia.** Klin. Monatsbl. f. Augenh. **136**:35-42, 1960.

In a previous communication (Klin. Monatsbl. f. Augenh. 134:563, 1959) the author reported on the "iris clip lens." In 30 patients with this lens, excellent compatibility was observed over periods of one and a half years. The main indication for intraocular lenses is uniocular aphakia. The lenses are inserted in a second procedure at least three months after uncomplicated cataract extraction. The presence of one or more surgical iris colobomas is mandatory to prevent pupillary block after insertion of the lens. The lens is treated by various aseptic measures prior to surgery. The preparation of the eye for this type of surgery and the postoperative treatment are discussed. Ocular reaction to the foreign body is kept to a minimum by pre- and postoperative administration of vasoconstrictors and steroids. The technique of implantation is outlined. (3 figures, 1 table, 6 references)

Gunter K. von Noorden.

Bonavolontà, A., De Beradinis, E. and Bonavolontà, G. **First observations on enzygmatic zonulolysis of Barraquer in cataract extraction.** Ophthalmologica **138**:370-377, Nov., 1959.

The authors base their discussion of this new procedure on their experience in 55 cases of various types of cataract. The age of the patients ranged from 16 to 86 years. The analysis of their data leads the authors to the conclusion that the method constitutes a technical innovation which deserves an important place in the surgery for cataract. (1 table, 1 reference)

F. H. Haessler.

Friede, R. **Preliminary work and positive experiments on artificial absorption of senile cataract without operation.** Klin. Monatsbl. f. Augenh. **136**:43-52, 1960.

Stimulated by reports on spontaneous absorption of cataractous lenses, the author experimented in animals with various chemicals which were injected into the lens. Some of these components had definite lentolytic action. Among the chemicals used was highly diluted acetic acid and urea. Acetic acid was employed in one human eye and the injection led to absorption of the cataractous lens. The technique of this procedure, which is still in an experimental stage, is described.

Gunter K. von Noorden.

Hoffmann, R. **Hemorrhage into the lens.** Klin. Monatsbl. f. Augenh. **135**:843-844, 1959.

This rare complication was observed after a perforating corneal injury. The hemorrhage occurred into the lens rather than into the anterior chamber. (1 figure, 2 references) G. K. von Noorden.

Kaiser, W., Loewe, I. and Ponsold, W. **A differential diagnostic possibility in evaluation of hypocalcemic lens opacities.** Klin. Monatsbl. f. Augenh. **136**:65-74, 1960.

The authors have developed a function test for the parathyroid gland. Infusion of ethylene-diamine-tetraacetic acid will result in temporary decrease of the serum calcium level. An unimpaired gland will respond quickly and restore the calcium level to normal. Glandular insufficiency, however, causes delayed recovery of the normal serum calcium level.

In 75 percent of the patients in whom parathyroid insufficiency was diagnosed by means of this test, hypocalcemic lens opacities of various degrees were noted. The test is a valuable diagnostic aid in lenticular opacities of unknown etiology. The importance of energetic antitetanic therapy is emphasized. (2 figures, 31 references) Gunter K. von Noorden.

Lugossy, C. **Cataract operations with alphachymotrypsin and erysiphake. Preliminary report.** Acta ophth. **38**:16-18, 1960.

In 187 successful cataract operations alphachymotrypsin was found to have an elective zonulolytic effect without damaging the capsule or the vitreous. (19 references) John J. Stern.

Strajber, Z. **Graefe knife incision in cases with shallow anterior chamber.** Klin. Monatsbl. f. Augenh. **135**:827-829, 1959.

Injury of the iris is a frequent complication when the Graefe knife enters a shallow chamber. The author, therefore, increases the depth of the chamber by injecting a small amount of saline solution through the limbus into the chamber just prior to surgery.

G. K. von Noorden.

11

RETINA AND VITREOUS

Ashton, Norman. **Diabetic retinopathy: a new approach.** Lancet **2**:625-630, Oct. 24, 1959.

Ashton suggests that in future research

this concept be considered, namely that failure of osmoregulation results in an increase of retinal turgescence because the retina has a higher glycolytic rate than almost any other tissue. This turgescence impedes the capillary circulation and results in stagnation and anoxia. Microaneurysms develop as a consequence of the metabolic disturbance.

F. H. Haessler.

Battistini, A. **Report of sex differences in the retinopathy of a group of 243 diabetics.** Arch. di ottal. **63**:379-383, Sept.-Oct., 1959.

Of 90 diabetic men, 38.8 percent had retinopathy and of 153 women, 41.1 percent had this lesion. Many references in the literature have shown that women have diabetic retinopathy before men do. This would not mean that sex has any particular effect on the disease or on the prevention of retinopathy after a given duration of time, because there may be other variables. (3 tables, 17 references)

Paul W. Miles.

Custodis, E. **Surgical therapy of retinal detachment: complications after scleral buckling by plastic implants.** Klin. Monatsbl. f. Augenh. **135**:769-775, 1959.

Among the factors enhancing tissue reaction and inflammation after retinal surgery are: intensity of diathermy and size of diathermized area, tissue irritation by the plastic material, foreign body reaction and local pressure damage by the implant, and a temporarily marked increase of intraocular pressure. Limitation of diathermy to the sclera directly overlying the retinal tear, intraoperative diamox injections, and rigid sterile technique combined with antibiotic therapy are thought to decrease the number of complications. It is of great importance to observe the anterior chamber postoperatively in order to recognize and treat an iritis in its initial stage.

Severe inflammatory reactions following surgery were observed in ten out of 136 patients; in some of them the plastic material had to be removed. Other complications and their management are discussed, among them: conjunctival dehiscences, diplopia, and thrombosis of the central retinal vein. The latter complication was observed in only two out of 1,000 patients. The author considers closure of the retinal hole or tear as the primary goal in retinal surgery. (1 table)

G. K. von Noorden.

François, J. and Neetens, A. **The sheathing of retinal veins in multiple sclerosis.** Ophthalmologica **138**:322-330, Nov., 1959.

Sheathing of the retinal veins may be a diagnostic sign which leads to the recognition of multiple sclerosis but is much less common than some statistics lead one to suppose. The sheathing is not the result of an inflammatory process but more probably the result of accumulation of products of disintegration of nervous tissue. (2 figures, 30 references)

F. H. Haessler.

Küper, J. **Familial sector-shaped retinitis pigmentoso.** Klin. Monatsbl. f. Augenh. **136**:97-102, 1960.

The case history of five members of one family are reported. Since only segments of the retina were involved, an ERG response was obtained. The dark adaptation curve did not show as extensive anomalies as those usually seen in diffuse pigment degeneration. (4 figures, 11 references)

Gunter K. von Noorden.

Lieb, W. A. Geeraets, W. J. and Guerry III, D. **Sickle-cell retinopathy.** Acta ophth. Supplement 58, 1959.

Of 65 patients with sickle-cell disease, 32 showed characteristic eyeground changes, ranging from tortuosity of the retinal vessels to retinitis proliferans and

central vein occlusion; an additional 26 patients showed scleral icterus or stasis and teleangiectasis of the conjunctival vesels or both. Patients with S-S hemoglobin and with sickle-cell hemoglobin C disease generally show similar pathologic changes. Patients with sickle-cell trait (S-A) have minor or no fundus changes. A direct relationship exists between the severity of the disease and fundus pathology. Coagulation of newly-formed retinal vessels may prevent massive vitreous hemorrhages. Carbonic anhydrase inhibitions are being studied for their effect on oxygenation of hemoglobin.

John J. Stern.

Meyerson, Louis. **Degeneratio punctata albescens.** Brit. J. Ophth. **43**:635-637, Oct., 1959.

A case of degeneratio punctata albescens with a family history of night blindness and peripheral constriction of the visual fields is presented.)3 figures, 3 references) Irwin E. Gaynon.

Rodriguez Barrios, R., Martinez Recalde, E., Mendilaharzu Carlos, and Mendilaharzu Celica. **Surgical rotation of the eyeball.** Brit. J. Ophth. **43**:584-595, Oct., 1959.

Surgical rotation was performed as an adjunct to the usual scleral buckling procedure in five cases of massive retinal detachment and disinsertion in the superior part of the retina. The four recti are separated from the globe. The eyeball was then rotated 90 degrees and the muscles resutured. The lateral rectus was sutured to the stump of the superior rectus.

The postoperative course was stormy. After a few months the eyes were reoperated and the eyeball was again rotated to its original position. The operation was successful in two cases. The motility of the rotated eye showed a dissociation between labyrinthine and voluntary movements and those of retinal origin. The former were normal, while the retinal stimulation had a 90-degree inclination. (12 figures, 15 references)

Irwin E. Gaynon.

Sobanski, J., Krawczyk, Z. and Swietliczko, I. **Clinical studies of the venous retinal pulse.** Klin. Monatsbl. f. Augenh. **135**:791-795, 1959.

According to ophthalmodynamometric studies the average diastolic blood pressure of the central retinal vein is 19 mm. Hg. It is recommended that one take the measurement at a moment when pulsation involves a larger portion of the vein and has reached the disc margin, rather than when the vein stem only is pulsating. This reduces the error of the method. The systolic blood pressure level of the central retinal vein is at 78 mm. Hg. (3 figures, 24 references) G. K. von Noorden.

Vannas, S. and Tarkkanen, A. **Chamber angle in retinal vein occlusion with glaucoma involved.** Acta ophth. **38**:50-56, 1960.

Gonioscopy was performed in 71 patients with total occlusion of the central retinal vein and in 58 in which a branch was occluded. In cases without simple glaucoma, the angle was wide open or only slightly narrowed, and no peripheral synechiae were seen. The findings in eyes with vein occlusion and simple glaucoma were the same. If the occlusion occurred in an eye with closed-angle glaucoma, corresponding gonioscopy findings were observed—peripheral synechiae—but never hemorrhagic glaucoma. Among the nine cases of hemorrhagic glaucoma both wide open angle and obliterated angle were observed. When a closed angle was seen, the opposite eye had a narrow angle. The chamber angle plays a secondary role in the development of hemorrhagic glaucoma. (2 figures, 19 references) John J. Stern.

13

NEURO-OPHTHALMOLOGY

Glew, W. B. **Progress of medical science: the pathogenesis of papilledema in intracranial disease; a review of some of the literature.** Am. J. M. Sc. **239**:221-230, Feb., 1960.

We call attention to this excellent review of the recent literature on the subject. (35 references) F. H. Haessler.

Montes Rodriguez, Carcar Crespi, and Cadierno Moreno. **A contribution to the etiology of homonymous hemianopsia.** Arch. Soc. oftal. hispano-am. **19**:874-892, Nov., 1959.

This is a tabulation of 24 cases of homonymous hemianopsia from a neuro-ophthalmologic department, comprising data relative to age, visual acuity, fundus findings, visual fields, pertinent symptoms, and etiology. Most interesting are the patients with homonymous congruent hemianopsia or quadrant anopsia following surgery for Parkinson's disease. This appears to be a new neurosurgical complication which should be considered by the neurosurgeon in establishing indications for surgery. Another prominent finding is the appearance of homonymous hemianopsia in diffuse intracranial processes, such as cerebral edema or intracranial hypertension without localization of the disease, and in circumscribed processes located at a distance from the retrochiasmal pathways. In such cases the campimetric data are of little localizing value. The author emphasizes the point that campimetric data are of diagnostic value only when integrated with the data of other examinations. (5 tables, 24 visual fields) Ray K. Daily.

14

EYEBALL, ORBIT, SINUSES

Bossalino, G. and Lovo, G. F. **A case of angio-fibro-sarcoma of the orbit.** Arch. di ottal. **63**:383-396, Sept.-Oct., 1959.

A man, 30 years of age, had painless congestion and exophthalmos of the right eye of 15 years duration. The vision was not stated. The orbit showed no tenderness. The right eye had five diopters of papilledema, and surrounding retinal edema and congestion. X-rays showed bone destruction below. The carotidograph showed compression. Treatment required eight operations. First the right internal carotid artery was ligated and then the right eye was enucleated. The orbit was explored and after biopsy exenterated and the eyelids were excised. A skin flap was brought down from the forehead for cosmetic repair. The angio-fibrosarcoma should be radiosensitive, but this tumor had gone too far. (7 figures, 5 references) Paul W. Miles.

Fine, B. S. and Zimmerman, L. E. **Postoperative mycotic endophthalmitis diagnosed clinically and verified histopathologically.** Brit. J. Ophth. **43**:753-758, Dec., 1959.

Mycotic endophthalmitis develops after a latent period of several days to months after surgery. A well localized abscess usually develops in the anterior segment. Corticosteroid therapy is temporarily beneficial. Enucleation is required as the disease progresses. Fungal elements are introduced at the time of intraocular surgery. In a patient observed by the authors myocotic endophthalmitis developed eight months after a successful intracapsular cataract extraction. No steroids were used at the time of surgery. The use of Mercorten, ACTH, Mycostatin, and potassium iodide were of no avail. (5 figures, 3 references) Irwin E. Gaynon.

Jacas, R., Ley, A. and Campillo, D. **Congenital intraorbital arteriovenous aneurysm.** J. Neurol. Neurosurg. & Psychiat. **22**:330-332, Nov., 1959.

The authors describe a case which illustrates the clinical picture of intraorbital

arteriovenous aneurysm, verified by angiography. (3 figures, 18 references)

F. H. Haessler.

Walser, E. **Twelve years experience with paladon implants in defects of the orbital margins.** Klin. Monatsbl. f. Augenh. **136**:89-92, 1960.

Paladon has been used in dentistry for a long time and is characterized by excellent tissue compatibility. The material was tolerated well in 30 out of 34 patients where it was used during plastic repair of defects in the bony orbit. Extrusion of the implant occurred in only four cases. This could not be ascribed to the character of the material, but rather to infection of the implant bed through a fistula from the paranasal sinus, or to compression atrophy of the skin. Gunter K. von Noorden.

15

EYELIDS, LACRIMAL APPARATUS

Barranco, Ruiz, F. **Treatment of palpebral epitheliomas.** Arch. Soc. oftal. hispano-am. **19**:893-899, Nov., 1959.

The difficulties and complications of irradiation and surgery for the destruction of palpebral epitheliomas are discussed, and the technique of cauterization with zinc chloride is described in detail. After thorough anesthesia in the surrounding healthy tissue the tumor is curetted completely away. Complete hemostasis is obtained by pressure or coagulation; the latter is brought about by the application of a saturated solution of zinc chloride to the surface for thirty seconds, the excess of which is neutralized with normal saline solution. In 22 cases of small tumor treated in this manner the results were entirely successful. In extensive lesions surgery followed by a free graft is indicated. (1 figure, 4 references)

Ray K. Daily.

Bauer, N. **A new method of dacryocystorhinostomy.** Szemeszet **96**:184-185, 1959.

The dacryocystorhinostomy devised by Fazakas has been modified by the author in such a way that the distal half of the sac is divided into two membranes, then drawn into the nose, stitched by two catgut sutures which also pass through the nasal mucosa and the nasal bone, whereby it is attached to the wall of the trepanation opening. Better results can be secured in this manner.

Gyula Lugossy.

Conrad, H. and Heinmueller, G. **Recurrent lid edema in children.** Klin. Monatsbl. f. Augenh. **135**:496-501, 1959.

Infestation with parasites such as trichinae, roundworms, and pinworms may lead to recurrent lid edema in children. Four cases are reported. Anaphylactic reactions are thought to be responsible for production of the clinical picture, which is compared with transient eosinophilic pulmonary infiltrations. (3 figures, 7 references)

Gunter K. von Noorden.

Crews, S. J. **Hydroa vacciniforme affecting the eye.** Brit. J. Ophth. **43**:629-634, Oct., 1959.

Hydroa vacciniforme is a recurrent vesicular eruption of the exposed cutaneous surfaces. Acitinic rays are the causative agent. The eruption is preceded by itching, red macules appear and later vesicles form. Pustules may develop. Such lesions may occur on the lids. Fine vesicles may develop in the interpalpebral portion of the cornea and finally a deep keratitis may develop. (3 figures, 21 references) Irwin E. Gaynon.

Fazakas, S. **Reconstructive surgery on an abnormally developed or displaced plica semilunaris for improvement of lacrimal drainage.** Klin. Monatsbl. f. Augenh. **135**:549-557, 1959.

Epiphora may be caused by congenital anomalies, traumatic lesions, or senile atrophy of the plica. Plastic procedures for reconstruction of the plica or its adjacent lacrimal grooves are discussed and illustrated. (11 figures, 11 references)

Gunter K. von Noorden.

Fazakas, S. **Diagnostic and therapeutic problems in stenosis of the lacrimal canaliculi.** Klin. Monatsbl. f. Augenh. **135**:691-696, 1959.

Dislocation of the puncta and direct or indirect narrowing of the lumen of the canaliculi are the most frequent causes of lacrimal obstruction. Obstruction of punctum or canaliculis may be congenital, as well as caused by papillomatous growths or mycotic material. Diagnostic and reconstructive procedures are discussed. (6 references)

Gunter K. von Noorden.

Fuchs, A. **Peculiar scars of the upper lid in China. Consequences of a hitherto unknown parasitic disease.** Klin. Monatsbl. f. Augenh. **136**:92-96, 1960.

The author observed these scars in the temporal aspect of the upper lid during his travels in China. The cause is unknown. It is surmised that parasites may be of etiologic significance.

Gunter K. von Noorden.

Hartmann, K. **Congenital entropion of both lower lids caused by epiblepharon.** Klin. Monatsbl. f. Augenh. **135**:835-839, 1959.

The literature on congenital entropion is reviewed. A case is reported in which entropion of the lower lids caused by epiblepharon was associated with an anomaly of the frenulum of the upper lip. (1 figure, 33 references)

G. K. von Noorden.

Huysmans, J. **Anthrax of the eyelids.** Ophthalmologica **138**:236-237, Sept., 1959.

While unloading a South-American ship carrying cattle hides, a 21-year-old Dutch stevedore was stung by an insect in the right upper lid. An ulcerative edematous lesion developed at the side of the sting, spreading rapidly from the third day on and becoming associated with high fever, malaise, and dyspnoea on the fourth day. A small dark spot at the bottom of the ulcer suggested anthrax; smears revealed typical anthrax bacilli. On combined penicillin-steroid therapy the general condition improved rapidly and the patient became afebrile. The primary lesion took the course of a typical anthrax carbuncle, not noticeably influenced by the antibiotic therapy. When the widespread necrosis of skin and deeper lid tissues caused ectropion a tarsorrhaphy was performed. The final outcome, cosmetically as well as functionally, was quite satisfactory without any plastic surgery.

Peter C. Kronfeld.

Junghannes, K. **Rare lid deformities caused by conjunctival pemphigus.** Klin. Monatsbl. f. Augenh. **135**:831-835, 1959.

Bilateral severe deformities of the upper lid were observed in a 50-year-old woman. The clinical course and subsequent histologic examination of excised tissue confirmed the diagnosis of conjunctival pemphigus. (3 figures, 30 references)

G. K. von Noorden.

Lemtis, H. and Neubauer, H. **Ankyloblepharon filiforme et membraniforme adnatum.** Klin. Monatsbl. f. Augenh. **135**: 510-516, 1959.

A patient was observed with bilateral manifestation of this rare anomaly. The adhesions were removed by electrosurgery. Three close relatives of the baby had complete cleft palates. A possible association of the two conditions has been pointed out by previous observers. (3 figures, 33 references)

Gunter K. von Noorden.

Lovo, G. F. **Suggestions on surgical reconstruction of lost tissue after removal of eyelid neoplasms.** Arch. di ottal. **63**: 361-379, Sept.-Oct., 1959.

The basal cell epithelioma is the most common neoplasm of the eyelids and is commonly on the lower eyelid. It is malignant locally but does not metastasize until late. It is radiosensitive but should be removed surgically for diagnosis before irradiation. The author attributes his good results to the use of pressure dressings to prevent vascularization, antibiotics before and after operation, and to meticulous care in technique. Two patients in his series had an en bloc replacement of tissue of the lower eyelid by tissue from the anterior lip of the ear just above the tragus. The cosmetic result in the ear is not illustrated. (8 figures, 17 references) Paul W. Miles.

Pohlig, G. **Treatment of dacryocystitis by filling the lacrimal sac with sulfonamide gel.** Klin. Monatsbl. f. Augenh. **135**: 577-579, 1959.

In acute dacryocystitis the sac is filled and sealed daily with the drug which is injected through a lacrimal canula. In congenital nasolacrimal stenosis the canula can be used as a probe. When unintentional perforation occurs a small amount of the drug is injected and a spread of infection prevented. (3 references) Gunter K. von Noorden.

Smith, W. Hamilton, Howsam, K. G. and Billings, J. J. **Epiphora, a symptom of early hypothyroidism.** Brit. J. Ophth. **43**:622-628, Oct., 1959.

Five cases of epiphora with puffiness of the eyelids are presented. The serum cholesterol was increased and the basal metabolic rate was decreased. Response to thyroid extract was good. (10 figures, 5 references) Irwin E. Gaynon.

Urrets-Zavalía, A. Jr. **V-Z procedure for the correction of senile ectropion.** Brit. J. Ophth. **43**:521-527, Sept., 1959.

There are some cosmetic objections to the results in the frequently-used techniques of repair of senile ectropion which are possibly eliminated in a new procedure which the author describes. The operation is done under the usual local anesthesia. A V excision of the full thickness of the lid is made at its worst area. This defect is now closed tightly and precisely with a tongue-in-groove approximation at its upper edge. Two parallel cuts are made from the skin incision in a Z formation at an angle of 60 degrees. This vertical Z incision is then transposed and sutured together as a horizontal Z, thus preventing any disfiguration of the repair of the V section. This technique is also suggested for lacerations, colobomata, tumor excisions, and senile-spastic entropion. (5 figures, 13 references) Morris Kaplan.

Valu, L. **Canaliculodacryocystostomy.** Szemeszet **96**:186-187, 1959.

A new operation is described for congenital partial atresia of the canaliculus. The closed part is exised and the free end is connected with the lacrimal sac. Gyula Lugossy.

Valu, L. **Canaliculodacryocystostomy.** Ophthalmologica **138**:378-380, Nov., 1959.

The author describes a new surgical procedure for the correction of congenital partial obliteration of the tear duct. After excision of the closed segment of the duct its open end is led into the lacrymal sac and secured with four suture. (1 figure, 6 references) F. H. Haessler.

Wilczek, M. **A simple operative method for lagophthalmos.** Klin. Monatsbl. f. Augenh. **135**:545-548, 1959.

A silk suture is inserted subcutaneously along the upper and lower lid margins. The suture is anchored to the periosteum

medially and laterally as well as crossed at the medial and lateral canthus. The suture is then tied at the lateral canthus. This results in narrowing of the palpebral fissure. The author observed excellent results in several cases treated by this method. (6 figures, 6 references)

Gunter K. von Noorden.

16
TUMORS

Garrett, Michael. **Ocular metastasis from seminoma.** Brit. J. Ophth. **43**:759-761, Dec., 1959.

A case of subconjunctival metastasis of a seminoma of the testicle is reported. The lesion responds to X-ray therapy. (3 figures, 6 references)

Irwin E. Gaynon.

Hirsch. O. **Life-long cures and improvements after transphenoidal operation of pituitary tumors.** Acta ophth. Supplement 56, 1959.

Out of a large number of patients operated upon by the author before 1938 in Europe, the status of 33 could be checked after 20 years or more. They all were cured or improved or had died from unrelated causes more than 20 years after the operation. John J. Stern.

Mathur, S. P. and Mathur, B. P. **Trichoepithelioma of the eyelid.** Brit. J. Ophth. **43**:762-763, Dec., 1959.

Three cases of epithelioma adenoides cysticum are described. It is rare, usually congenital although it may not appear until puberty, frequently hereditary, and it may become locally malignant. The lesion may reappear at a different site. (4 references) Irwin E. Gaynon.

Valu, J. **Astigmatism with consecutive amblyopia caused by multiple lipoma of the orbit.** Klin. Monatsbl. f. Augenh. **135**:820-822, 1959.

In a 36-year-old woman high astigmatism and amblyopia persisted in the involved eye after removal of the causative tumor. In view of his findings the author urges removal of such lesions in early childhood to prevent development of astigmatism and irreparable amblyopia. (1 figure, 4 references)

G. K. von Noorden.

17
INJURIES

Chaussé, C., Payrau, P. and Raynaud, G. **Localization of orbital foreign bodies by the method of stereo-radiographic transposition of Chaussé.** Ann. d'ocul. **193**:194-223, March, 1960.

The authors describe a system of stereoradiography for the localization of intraorbital foreign bodies. Two X-ray films are exposed from slightly displaced positions and the films then viewed stereoscopically. The geometric and other mathematical analyses are illustrated. A contact lens with graticules is used to center the eye and for exact measurement. The authors feel that this method is superior to that of Sweet for localization. A minor limitation is the need for good stereopsis on the part of the examiner. The writers feel that this can be acquired with practice by any ophthalmologist with good binocular vision. (11 figures, 49 references) David Shoch.

Law, T. B. **Two unusual eye accidents.** M. J. Australia **1**:50-51, 1960.

An automobile accident caused destruction of the left eye but no glass entered the orbit, whereas the right eye suffered no damage but 25 pieces of windscreen glass lodged deep in the orbit.

A child fell with a drinking glass causing a large cut through sclera with prolapse of ciliary body and vitreous. After repair the eye appeared to recover fully.

Ronald Lowe.

Luntz, M. **Transient traumatic myopia**

with hypotension. Brit. J. Ophth. **43**:565-571, Sept., 1959.

The appearance of myopia after traumatic chamber loss with hypotension and no other ocular pathologic change has been reported very rarely. A 32-year-old woman, after a blow struck one eye, had a flat chamber and hypotension of 11 with no other signs of damage except a myopia of three diopters which persisted for two weeks and then apparently healed completely. The literature of this syndrome is reviewed but no satisfactory explanation for this picture is arrived at. (24 references) Morris Kaplan.

Oksala, A. **Copper fragments in anterior chamber and vitreous diagnosed by ultrasound.** Klin. Monatsbl. f. Augenh. **136**: 81-88, 1960.

The case of a patient is reported in whom copper fragments were present in the anterior chamber of one eye and in the vitreous of the fellow eye. The foreign bodies could be localized with the ultrasound method. The results corresponded with X-ray localization. Ultrasound is also of great value in localization of intraocular foreign bodies which are not radioopaque. The echo yielded by a foreign body can easily be distinguished from echos produced by other intraocular pathologic conditions. (10 figures, 5 references) Gunter K. von Noorden.

Solarès, A. **Cranial contusion and the uveomeningeal syndrome.** Arch. d'opht. **19**:721-729, Oct.-Nov., 1959.

The author reports the case of a young male patient of 16 years who fell from a truck with resultant major head injury. A week later he developed bilateral visual disturbances. His fundi showed disseminated hemorrhages, perivasculitis, hyperemia of the discs, cotton-wool exudates, and a possible retinal tear in one eye near the equator, with vitreous exudates. The course of the disease suggested the uveomeningeal syndrome but there were no associated ectodermal changes. Lumbar puncture was refused. The report concludes with a consideration of the syndromes of Vogt-Koyanagi and Harada. Solarès questions whether or not trauma and toxic influences may play a role in the etiology. (23 references) P. Thygeson.

18

SYSTEMIC DISEASE AND PARASITES

McLean, Charles M. **Ocular onchocerciasis in northern Ghana. A treatment survey.** Brit. J. Ophth. **43**:477-485, Aug., 1959.

The diagnosis of onchocerciasis was made by skin biopsy in 43.4 percent of the cases, palpable nodules in 65.6 percent, skin changes in 75 percent, microfilariae in the anterior chamber in 38.6 percent and in 84.5 percent of the cases there were ocular signs such as corneal opacities, optic atrophy, chorioretinal degeneration, posterior synechiae, cataracta complicata, cupped discs, and phthisis bulbi. Most of the patients were emaciated and also had bilharzia.

Antrypol was found to be too toxic for mass therapy. Banocide is safe. The side reactions are controlable with antihistamines. Both drugs produced an improvement in vision and have a microfilarcidal action. (4 references) Irwin E. Gaynon.

Thomas, C., Cordier, J., Larcan, A. and Streiff, F. **Ophthalmologic manifestations of the macroglobulinemia of Waldenström.** Arch. d'opht. **19**:609-619, Sept., 1959.

The dysglobulinemias constitute a new order of disease entity with numerous visceral manifestations. In 1944 Waldenström noted the existence of macroglobulins in the serum of patients with lymphoid cryptoleucosis; since 1944 more than 200 such cases have been reported. The

authors of the present report have observed seven cases of the macroglobulinemia of Waldenström and describe eye manifestations in four of them. In an extensive review of the literature on dysglobulinemia, they note that retinal hemorrhages, tortuous, dilated veins of irregular calibre, fine white exudates, and disturbances in retinal hemodynamics (including systolic arterial pulsations) have all been reported, as well as rare instances of papilledema. They conclude that all the dysglobulinemias show similar eye changes due to damage of vessel walls by the abnormal globulins. They propose that the term "dysproteinemic fundus" be used to designate this clinical entity. P. Thygeson.

19

CONGENITAL DEFORMITIES, HEREDITY

Darabos, G. and Vörösmarthy, D. **Septum canalis nervi optici.** Ophthalmologica **138**:347-349, Nov., 1959.

The authors describe doubling of the optic canal with narrowing of its lumen and atrophy of the optic nerve. (1 figure, 6 references) F. H. Haessler.

Gassler, H. and Berthold, H. **A contribution to ectodermal dysplasia from the ophthalmologic viewpoint.** Klin. Monatsbl. f. Augenh. **136**:52-65, 1960.

This defect is characterized by oligodontia, malfunction or absence of sweat and sebaceous glands, absence of finger or foot nails, and congenital malformations of cornea and iris. Three cases are reported. Two of these patients had mesodermal chamber angle anomalies as well as atrophy of the iris stroma. This was associated with pupillary malformation and buphthalmos in one patient. The exact etiology of this condition is unknown, however, damage to the embryo between the sixth and seventh fetal month must be assumed to play a role in the production of this syndrome. (7 figures, 2 tables, 45 references) Gunter K. von Noorden.

Grützner, P. **Eye symptoms in ataxia teleangiectatica (Louis-Bar's syndrome).** Klin. Monatsbl. f. Augenh. **135**:712-717, 1959.

This syndrome is characterized by cerebellar ataxia and teleangiectases of the conjunctiva and the external ear. A case in an eight-year-old boy is reported. The disease belongs to the phakomatoses, and, within this group, seems to be closely related to the von Hippel-Lindau's syndrome. (1 table, 8 references)
Gunter K. von Noorden.

Heidensleben, E. **Hereditary congenital koilonychae accompanied by syndermatotic cataract.** Acta ophth. **38**:1-4, 1960.

A case of this disturbance is presented and the possibility of general ectodermal dysplasia discussed. (1 figure, 9 references) John J. Stern.

Misar, R. **The occurrence of osseous tissue in a malformed eye.** Klin. Monatsbl. f. Augenh. **136**:74-81, 1960.

Embryonic bone tissue was found in the retrolental membrane of a severely degenerated globe. Case history and histologic studies are reported. Examination of the specimen revealed the presence of several malformations. Among them were: hyperplasia of the primary vitreous, persistent tunica vasculorum lentis, dysplasia retinae simplex, and proliferation of nerve fibers into the vitreal space. The formation of bone tissue has not been reported before in this connection. (6 figures, 5 references)
Gunter K. von Noorden.

Oliveira, H. M. and Goncalves, R. P. **Study of an albino eye.** Arq. brasil de oftal. **22**:54-59, 1959.

There have been few histological studies of the albino eye. The authors present

a case history with an illustrated report of the histologic findings of the eye of an albino negro who died of generalized carcinomatosis. Other instances of albinism had been observed in this patient's family. The impaired visual acuity is ascribed to an anomaly in the macular region and the deficiency of pigment. Excess light does not produce any retinal alteration. Contrary to other investigators, they were unable to observe pigment in any ocular structure. Detailed study of serial sections failed to localize the macular zone. (6 microphotographs, 3 references) James W. Brennan.

Sebestyén, J. **Diffuse familial chorioretinal atrophies. (Atrophy gyrata of choroid and retina complicated by cataracta calcarea).** Ophthalmologica **138**: 336-346, Nov., 1959.

Sebastyén discusses familial chorioretinal atrophy and reports two cases of it which were complicated by calcareous cataract. The calcification of the lens is presumably a part of a local metabolic circulatory disturbance in an embryonally damaged lens. (4 figures, 36 references) F. H. Haessler.

Velický, G. **Contribution to the study of congenital blindness.** Ophthalmologica **138**:330-335, Nov., 1959.

The author describes the case of a woman who had two normal children in her first marriage and three blind children who had all manifestations of the Kurz syndrome with congenital blindness in the second. They had a hypermetropia of eight diopters, complete or partial blindness, enophthalmos, inactive pupils, restricted ocular movements and normal eyegrounds. The margins of the left orbit were aplastic and the orbit itself was underdeveloped. (1 figure, 5 references) F. H. Haessler.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Münchow, W. **Seventy-five years of local anesthesia.** Klin. Monatsbl. f. Augenh. **136**:106-111, 1960.

Topical anesthesia with cocaine was introduced by Carl Koller in 1884. The circumstances of this discovery, as well as procedures in use prior to the introduction of cocaine, are reviewed. (21 references) Gunter K. von Noorden.

Schweitzer, N. M. J. **A glaucoma department.** Ophthalmologica **138**:233-236, Sept., 1959.

The organization and current activities of a special glaucoma clinic incorporated in the hospital for eye diseases of the University of Utrecht (The Netherlands) are described. The critical problems of standardization of equipment and methods of examination have been largely solved. The Goldmann perimeter and certified tonometers are used throughout. For tonography there are available electronic tonometers manufactured by V. Mueller in Chicago or Schwarzer in Munich. A satisfactory recorder has been obtained by combining a D-C preamplifier, type Philips GM4531 with an inexpensive "helcoscriptor" of the Hellige Co.

The clinic staff consists of a senior staff member (the "superintendent") and several assistants. No mention is made of technical assistants or of social workers. The clinic keeps separate records.

Peter C. Kronfeld.

NEWS ITEMS

EDITED BY DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

DEATHS

Dr. Lynwood Kent Best, Charleston, South Carolina, died January 19, 1960, aged 55 years.

Dr. Maurice Elias Mesirow, San Francisco, California, died January 29, 1960, aged 73 years.

ANNOUNCEMENTS

ORTHOPTIC EXAMINATIONS

The annual examination of orthoptic technicians by the American Orthoptic Council will be conducted in August and October, 1960.

The written examination will be nonassembled and will take place on Thursday, August 18th, in certain assigned cities and will be proctored by designated ophthalmologists.

The oral and practical examinations will be on Saturday, October 8th, in Chicago, just preceding the meeting of the American Academy of Ophthalmology and Otolaryngology.

Application for examination will be received by the office of the chairman of examinations, Dr. Frank D. Costenbader, 1605 22nd Street, N.W., Washington 8, D.C., and must be accompanied by the examination fee of $30.00. Applications will not be accepted after July 1, 1960.

MOUNT SINAI COURSE

The Mount Sinai Hospital of New York City together with Columbia University is giving a course in "The diagnosis and management of glaucoma" from October 18 to November 8, 1960. Gonioscopy and tonography will be stressed. Complete information may be obtained from the Registrar for Medical Instruction, The Mount Sinai Hospital, 1 East 100th Street, New York City.

MISSIONARY OPHTHALMOLOGIST NEEDED

The Christian Medical College of Ludhiana, Punjab, India, needs a full-time missionary ophthalmologist to build up the Department of Ophthalmology which is already functioning well. Such a person would have an important work, under rather restricted financial limitations, in teaching undergraduate and graduate nursing and medical students. Research would be one of the important fields of service. For further information write to Dr. Melvin A. Casberg, director, Christian Medical College, Ludhiana, Punjab, India.

WANTED WORKERS IN INDIA

Dr. Tulsi Das, director of Medical Education, Chandigarh, Punjab, India, is in need of (1) an ophthalmic pathologist, (2) an ophthalmic virologist, (3) a biochemist with ophthalmic experience (if possible), and (4) a bacteriologist. These specialists should have the highest qualifications to conduct research. First-class fare and a salary sufficient for satisfactory livelihood will be provided, preferably for service of three years or longer.

COLORADO COURSE

The Colorado Ophthalmological Society and the Division of Ophthalmology of the Department of Surgery and the Office of Postgraduate Medical Education, The University of Colorado School of Medicine, will cosponsor a postgraduate course on "Internal ophthalmology," at Aspen, Colorado, on July 5th, 6th, 7th and 8th. Guest speakers will be Dr. F. Bruce Fralick, Dr. Michael J. Hogan, Dr. Albert N. Lemoine, Jr., and Dr. Albert D. Ruedemann. Members of the faculty of the University of Colorado School of Medicine who will participate in the program are Drs. C. Wesley Eisele, George A. Filmer, Ivan E. Hix, Jr., Harold C. Leight and James P. Rigg. Members of the program committee are Drs. George A. Filmer, John C. Long, Morris Kaplan, James C. Strong, Jr., and J. Leonard Swigert.

Further information may be obtained from the Office of Postgraduate Medical Education, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver 20, Colorado.

ASIA-PACIFIC ACADEMY

The first congress of the Asia-Pacific Academy of Ophthalmology, sponsored by the Philippine Ophthalmological Society, will convene in Manila on October 9th and will continue through October 13th. The program follows:

SUNDAY, October 9, 1960

9:00 A.M. to 12:00 NOON; 2:00 to 5:00 P.M. Registration of delegates, Science Hall, University of the Philippines, Medical Center.

8:00 P.M. Reception for Delegates, Guests and members of the A.P.A.O., to be given by the President of the A.P.A.O.

MONDAY, October 10, 1960

8:00 A.M. Opening of commercial exhibits, Auditorium, Institute of Hygiene, Herran, Manila.

9:30 A.M. Opening ceremonies, Science Hall, University of the Philippines, Medical Center.

11:30 A.M. Picture taking of delegates, Science

Hall, University of the Philippines, Medical Center.

2:00 P.M. Guest lecturer—Dr. Joaquin Barraquer (Spain), Science Hall, University of the Philippines, Medical Center.

3:00 P.M. First meeting, House of Delegates, Science Hall, University of the Philippines, Medical Center.

3:00 to 5:30 P.M. Scientific sessions: Free papers and scientific films, University of the Philippines, College of Medicine, Lecture Halls.

TUESDAY, October 11, 1960

9:00 A.M. Guest lecturer, Dr. Saul Sugar, U.S.A., Science Hall, University of the Philippines, Medical Center.

10:00 A.M. to 12:00 NOON—scientific sessions—free papers and scientific films, University of the Philippines, College of Medicine, Lecture Halls.

2:00 P.M. Guest lecturer, Dr. Tulsidas (India), Science Hall, University of the Philippines, Medical Center.

3:00 to 5:30 P.M. Scientific sessions, free papers and scientific films, University of the Philippines, College of Medicine Lecture Halls.

WEDNESDAY, October 12, 1960

9:00 A.M. Guest lecturer, Dr. Geminiano de Ocampo (Philippines), Science Hall University of the Philippines, Medical Center.

10:00 A.M. to 12:00 NOON—scientific sessions—free papers and scientific films, University of the Philippines, College of Medicine, Lecture Halls.

2:00 P.M. Guest lecturer, Dr. Akira Nakajima (Japan), Science Hall, University of the Philippines, Medical Center.

3:00 P.M. Second meeting of House of Delegates, Science Hall, University of the Philippines, Medical Center.

3:00 to 5:30 P.M. Scientific sessions—free papers and scientific films, University of the Philippines, College of Medicine, Lecture Halls.

THURSDAY, October 13, 1960

9:00 A.M. Guest lecturer, Dr. Bruce Hamilton (Australia).

10:00 A.M. Guest lecturer, Dr. D. L. McLaren (Africa). Science Hall, University of the Philippines, Medical Center.

2:00 P.M. Closing ceremonies.

3:00 to 5:00 P.M. Excursion and tours.

8:30 P.M. Reception and ball to be given by the members of the Philippine Ophthalmological Society for the delegates, guests and members of the A.P.A.O. at the Manila Hotel Fiesta Pavilion, featuring Philippine Folk Dances.

Further information may be obtained by writing the Executive Committee, Asia-Pacific Academy of Ophthalmology, Clinica Tamesis, 42 Quezon Boulevard Extension, Quezon City, Philippines.

Societies

MASSACHUSETTS EYE AND EAR MEETING

Ophthalmic papers presented at the annual meeting of the Massachusetts Eye and Ear Infirmary Alumni Association held at the Infirmary, Boston, April 26th and 27th, included:

"The use of silicone in scleral buckling surgery," Charles L. Schepens; "Alloplastic anterior chamber drainage tubes in glaucoma," William Stone, Jr., and John Sebestyen; "Temporary esotropia due to systemic atropine," Bernard H. Zeavin; "Blackouts," David G. Cogan; "Experimental and clinical enzymatic debridement of the cornea," Gustav C. Bahn; "Retinopathy in primary hyperaldosteronism," William Beetham; "Therapeutic corneal grafts," Edward C. Sweebe and Claes-Hendrik Dohlman.

"Keratoacanthoma," Richard Chapman; "Clinical trial of 0.25-percent demecarium bromide," Jeremy B. Whitney; "Some diseases we used to see," Edwin B. Dunphy; "Allergic recurrences of ocular toxoplasmosis," Herbert Kaufman; "Central retinal artery occlusion: Case report with comments on therapy and pathophysiology," Firmon E. Hardenbergh; "Ocular changes in hydraencephaly," David G. Cogan, Kevin Hill and Philip Dodge; "A method of cataract delivery when alpha chymotrypsin is employed," Thomas Cavanaugh; "Cataract extraction with alpha chymotrypsin" (a movie), Gerald B. Kara.

"Pupillary block in aphakia," Paul A. Chandler; "Early senile cataract," Richard H. Dennis; "Acute glaucoma and the ERG," Benjamin Ziv; "New instrumentation in phakoerisis," Francis A. L'Esperance, Jr.; "Electromyography of the eye muscles: Clinical applications," Ingrid Gamstorp and Carl Kupfer; "Clinical experience with the Goldmann applanation tonometer," Raymond Harrison; "The ophthalmologist and contact lenses," William Stone, Jr.; "Herpes febrilis infections of the cornea," Michael J. Hogan.

PENNSYLVANIA-NEW JERSEY PROGRAM

On the ophthalmology program of the joint meeting of the Pennsylvania Academy of Ophthalmology and Otolaryngology and the New Jersey Academy of Ophthalmology and Otolaryngology, held at the Hotel Traymore, Atlantic City, May 19th, 20th and 21st were:

Edward A. Atwood, Paterson, New Jersey, presiding: "Symposium on clinical methods of examination," Charles M. Reel, Andrew deRoetth, Jr., Charles D. J. Regan and Carteret Lawrence; "Complications following lens extraction," John H. Dunnington; "Technique of indirect ophthalmoscopy," Charles D. J. Regan; "Contact lens fitting in office practice," Benjamin F. Souders, Irvin Levy and Frederick P. Sutliff; "Repair of corneal injuries," C. William Weisser; "Examining the pediatric eye patient," Frank D. Costenbader; "Ophthalmic anatomy," Dewey Katz; "Office management," H. Ford Clark, Harold D. Barnshaw and James H. Delaney.

"Refraction: Practical considerations," Alfonse A.

Cinotti, Bernard C. Gettes and William O. La Motte, Jr.; "Refinements in ophthalmic surgery," Abraham Schlossman; "Management of uveitis," John Schillieri, Henry N. Bronk and Irving H. Leopold; "Ophthalmological findings associated with systemic disease," Roscoe J. Kennedy; "Developments in space ophthalmology," Victory A. Byrnes; "Ophthalmodynamometry," Robison D. Harley. John K. Covey, Bellfonte, Pennsylvania, presided during the "Symposium on current ocular therapy," with Irving H. Leopold, Abraham Schlossman, Francis Furgiuele, and Leonard Apt participating.

Long Island society

Dr. Goodwin M. Breinin, New York, presented the paper of the evening at the April meeting of the Long Island Ophthalmological Society. The subject of Dr. Breinin's address was "The A and V syndromes."

Miscellaneous

Gill Congress

The Gill Memorial Eye, Ear and Throat Hospital, Roanoke, Virginia, has just completed its 33rd annual spring congress in ophthalmology and otolaryngology and allied specialties. More than 300 doctors and their wives attended. Forty states and Canada were represented. A total of 18 guest speakers gave 50 lectures during the five and one-half days of the meeting. In 1961, the 34th congress will be held from April 9th through April 14th.

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MATALENE

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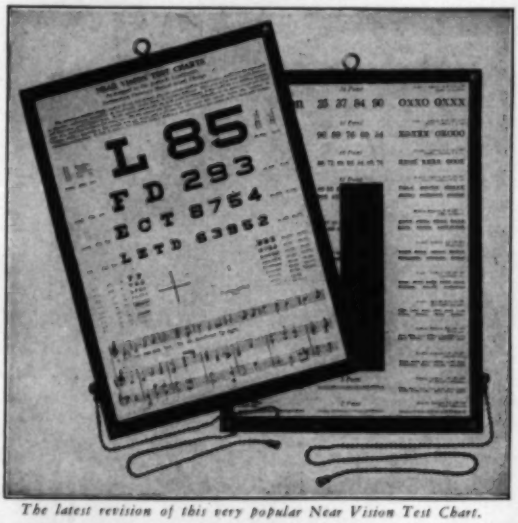

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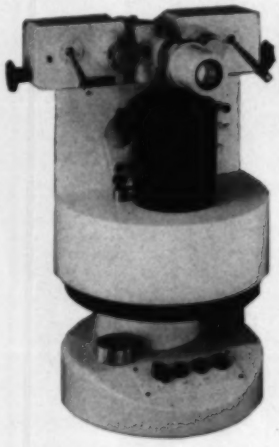

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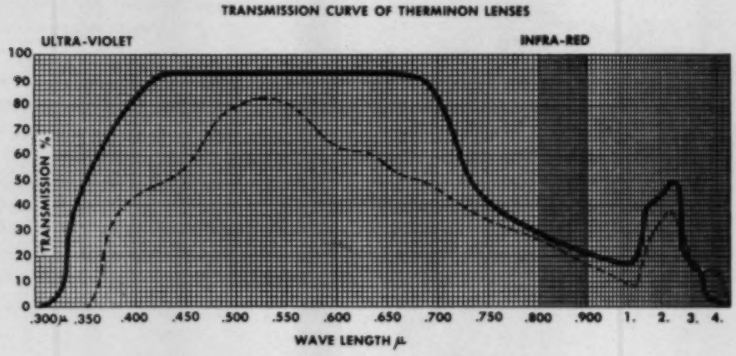

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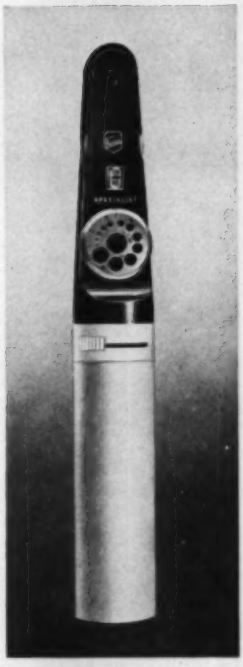

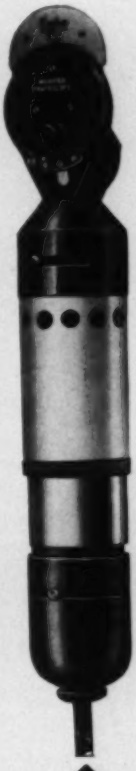

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